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DISEASES

of the

CHEST

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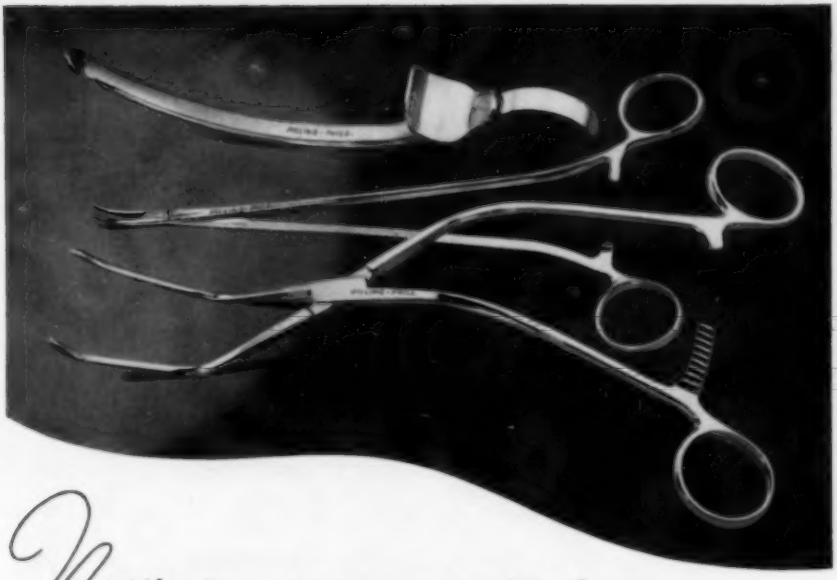

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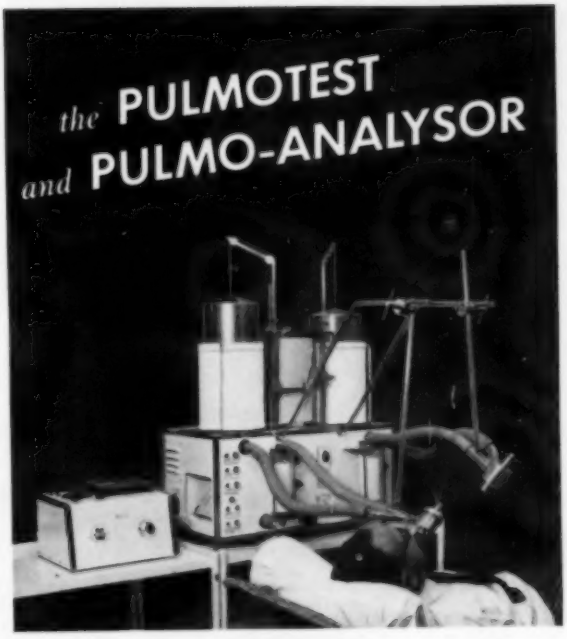

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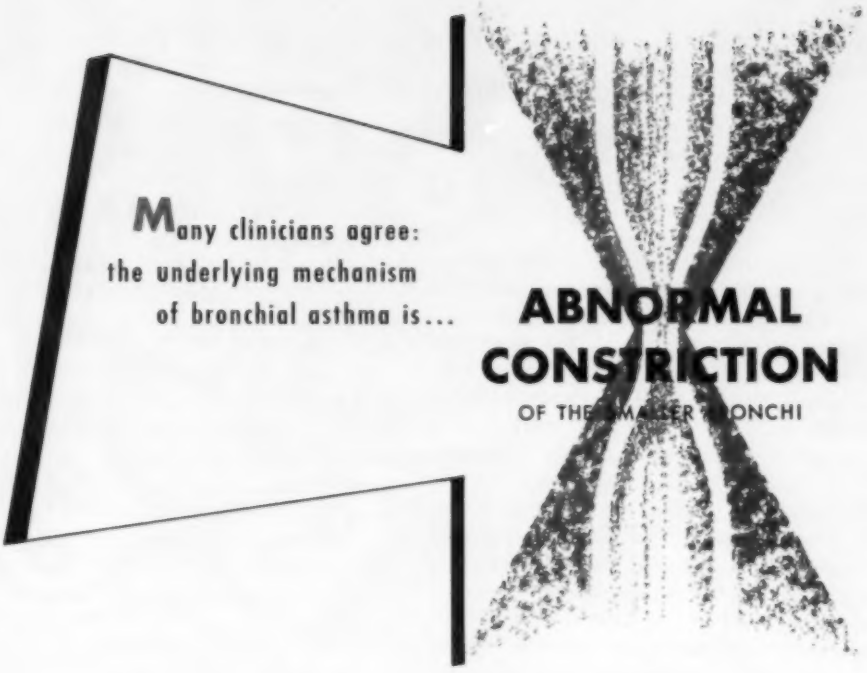

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Literature upon request

A Laboratory and Clinical Report on Adrenosem® Salicylate

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History

The first investigation of a hemostat with an action comparable to Adrenosem Salicylate was made by Derouaux and Roskam[1] in 1937. They reported that an oxidation product of adrenalin, adrenochrome (which has no sympathomimetic properties), has prompt hemostatic activity.

It was further found that various combinations of adrenochrome, notably the oxime and semicarbazone, produced stable solutions. But, these were so slightly soluble that sufficient concentration could not be obtained for practical therapeutic use. By combining these adrenochrome compounds in a sodium salicylate complex a stable, soluble form can be obtained. This complex has been given the generic name, carbazochrome salicylate, and is supplied under the trade name Adrenosem Salicylate.

Roskam, in his study entitled "The Arrest of Bleeding,"[2] enumerates "the drugs whose efficaciousness as hemostatics have been proved by accurate methods in experimental animals and in healthy men as well. . . . One is the monosemicarbazone of adrenochrome [Adrenosem Salicylate]."

Chemistry

Adrenosem Salicylate is a synthetic chemical. The full chemical name is adrenochrome monosemicarbazone sodium salicylate complex.

Pharmacology

Although it is chemically related to epinephrine, Adrenosem Salicylate has no sympathomimetic effects. It does not alter blood components, nor does it affect blood pressure or cardiac rate.[2-7]

(* U.S. Patent 2,581,850)

Sherber, in an early study,[3] concludes that Adrenosem Salicylate* "is a potent antihemorrhagic factor in those conditions in which the integrity of the smaller vessels is interrupted, and is superior to any similar material that is now available."

He continues, "From our experience it appears that adrenochromazone complex is indicated in preventing vascular accidents incident to hypertension; in maintaining small vessel integrity; in the preoperative preparation where oozing from a vascular bed is anticipated, as in tonsillectomies, adenoidectomies and prostatectomies; and as an adjunct in the treatment of bleeding from such surgical procedures."

Adrenosem Salicylate may be administered simultaneously (but separately) with any type of anesthetic, anticoagulant, or vitamin K and heparin.

A Unique Systemic Hemostat

Clinical investigators[2-7] are in agreement that Adrenosem Salicylate controls bleeding and oozing by decreasing capillary permeability and by promoting the retraction of severed capillary ends. It aids in maintaining normal capillary integrity by direct action on the intercellular "cement" in capillary walls. The interesting work of Fulton[8] confirms this. Adrenosem Salicylate, since it is not a vasoconstrictor, has no effect on large severed blood vessels and arterioles.

Adrenosem Salicylate is being used both prophylactically and therapeutically in thousands of hospitals, and in virtually every type of surgical procedure. It has also proved most useful in dental surgery.[7]

Owings reported on the use of Adrenosem Salicylate in controlling postoperative adenoid bleeding in 102 cases.[4] "We have used 2½ mg.

(½ ampule) intramuscularly, 15 minutes before anesthesia for children and 5 mg. (1 ampule) for adults." In only one patient did bleeding occur. Three others showed red blood from the nose and mouth. These patients "were then given 5 mg. intramuscularly, with prompt and complete control. We have also noticed that bleeding stopped more promptly on the operating table."

This is a 1% incidence of postoperative bleeding using Adrenosem Salicylate preoperatively, compared to an incidence of 10% postoperative bleeding in all cases taken from previous records, without Adrenosem Salicylate medication.

Peele reports on the use of Adrenosem Salicylate in treating 178 patients with 24 different conditions.[5] The drug was first used to control postoperative hemorrhage from the adenoid region. He adds: "The results were so dramatic that since that date [1953] Adrenosem Salicylate has been used postoperatively to reduce bleeding from all otolaryngologic and bronchoesophagolic procedures, to treat postoperative hemorrhage from the tonsil and adenoid regions, and to treat selected cases of epistaxis."

The effectiveness of Adrenosem Salicylate in controlling bleeding and oozing in 330 patients is reviewed by Bacala.[6] "Our experience of the effect of carbazochrome salicylate on 317 surgical indications and 13 obstetricogynecological conditions, has been therapeutically encouraging and successful for the control of capillary bleeding. Foremost among the cases studied were 223 tonsillectomies definitely benefited by this metabolic hemostat, making a diminution of the control incidence of posttonsillectomy bleeding of 19.8% down to 7%. It has also been found useful in gastro-intestinal bleeding, cataract extraction, epistaxis, incisional seepage, trans-urethral prostatectomy, menometrorrhagias, cervical ooze, antepartum and postpartum bleeding, threatened abortion, and prevention of capillary hemorrhages during hedulin or dicumerol therapy."

Side Effects

All investigators concur that, at recommended dosage levels, Adrenosem Salicylate is free from toxic effects. No cumulative effects attributable to the drug have been reported.

The only side reaction noted has been a transient stinging sensation in the area of injection when Adrenosem Salicylate is used intramuscularly. As one investigator comments: "The brief discomfort which attends the injection of Adrenosem into the gluteal region has not been a significant problem in children or adults as originally anticipated."[8]

Indications

Idiopathic purpura, retinal hemorrhage, familial telangiectasia, epistaxis, hemoptysis, hematuria.

Postoperative bleeding associated with:
tonsillectomy, adenoidectomy and
nasopharynx surgery;
prostatic and bladder surgery;
uterine bleeding;
postpartum hemorrhage;
dental surgery;
chest surgery and chronic pulmonary bleeding.

Dosage

For recommended dosage schedules, please send for detailed literature.

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Tablets: 1 mg. S.C. Orange, bottles of 50.
Tablets: 2.5 mg. S.C. Yellow, bottles of 50.
Syrup: 2.5 mg. per 5 cc. (1 tsp.), 4 ounce bottles.

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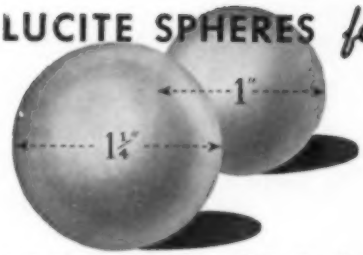

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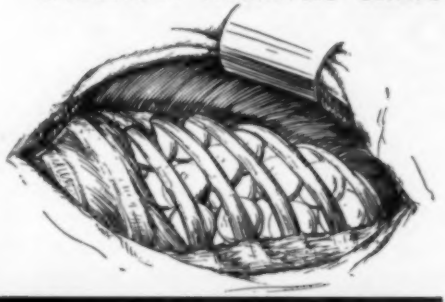

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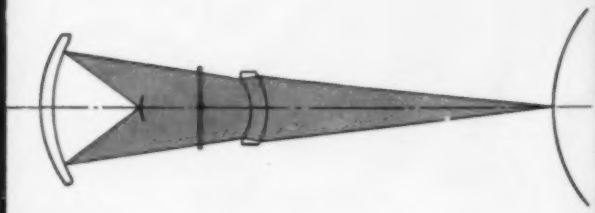

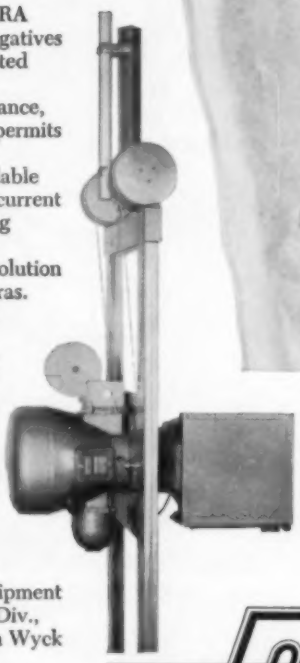

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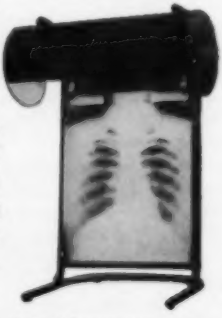

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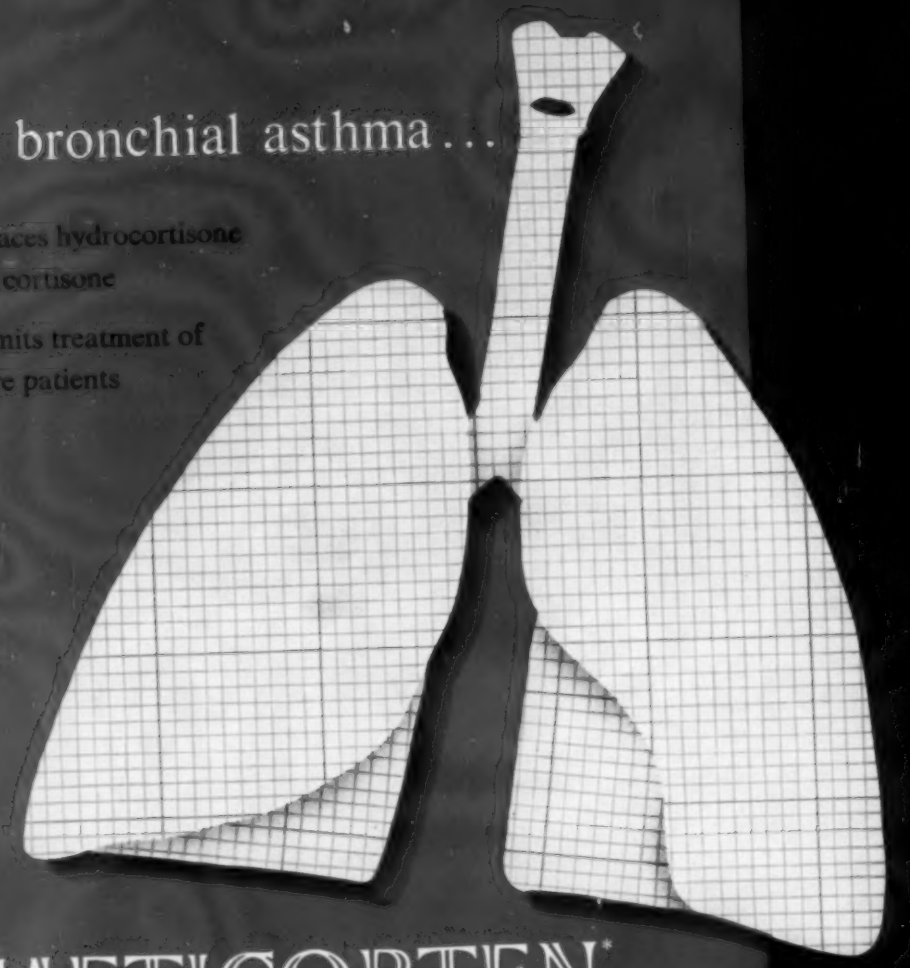

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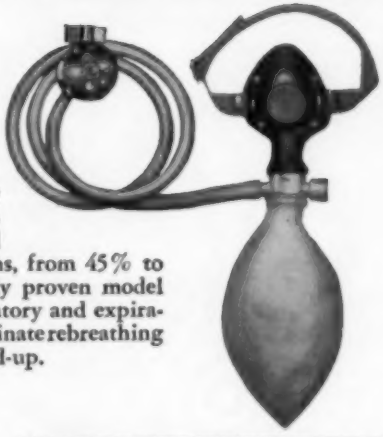

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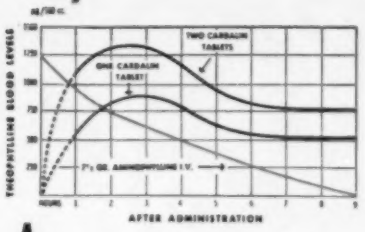

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(Adapted from Bickerman, H. A., et al.: Ann. Allergy 11:301, 1953, and Truitt, E. B., Jr., et al.: J. Pharmacol. & Exper. Therap. 100:309, 1950.)

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Bickerman, H. A., et al.: Ann. Allergy 11:309, 1953.

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Barach, A. L., et al.: Dis. of Chest 23:121, 1953.

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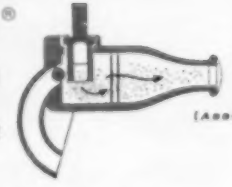

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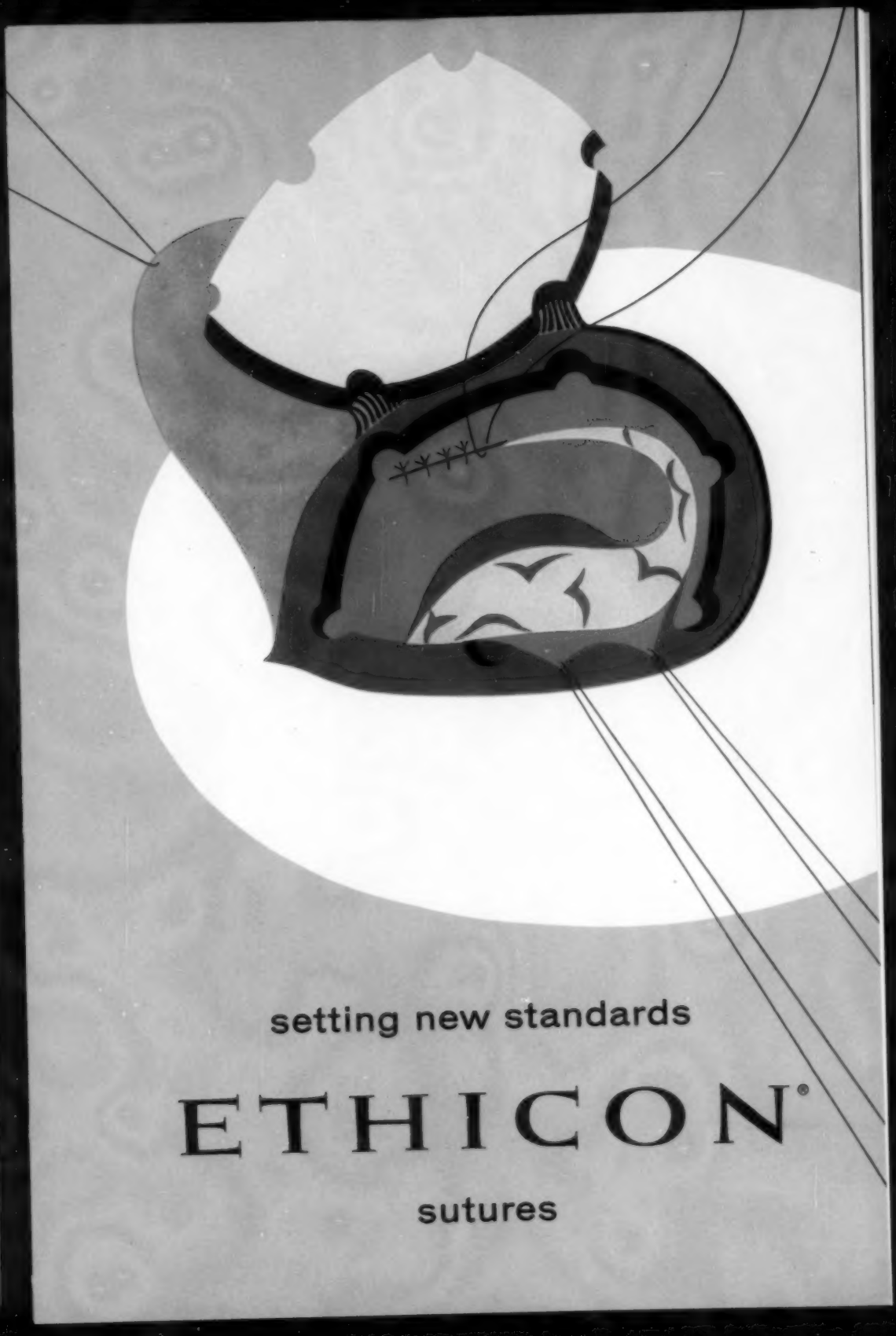
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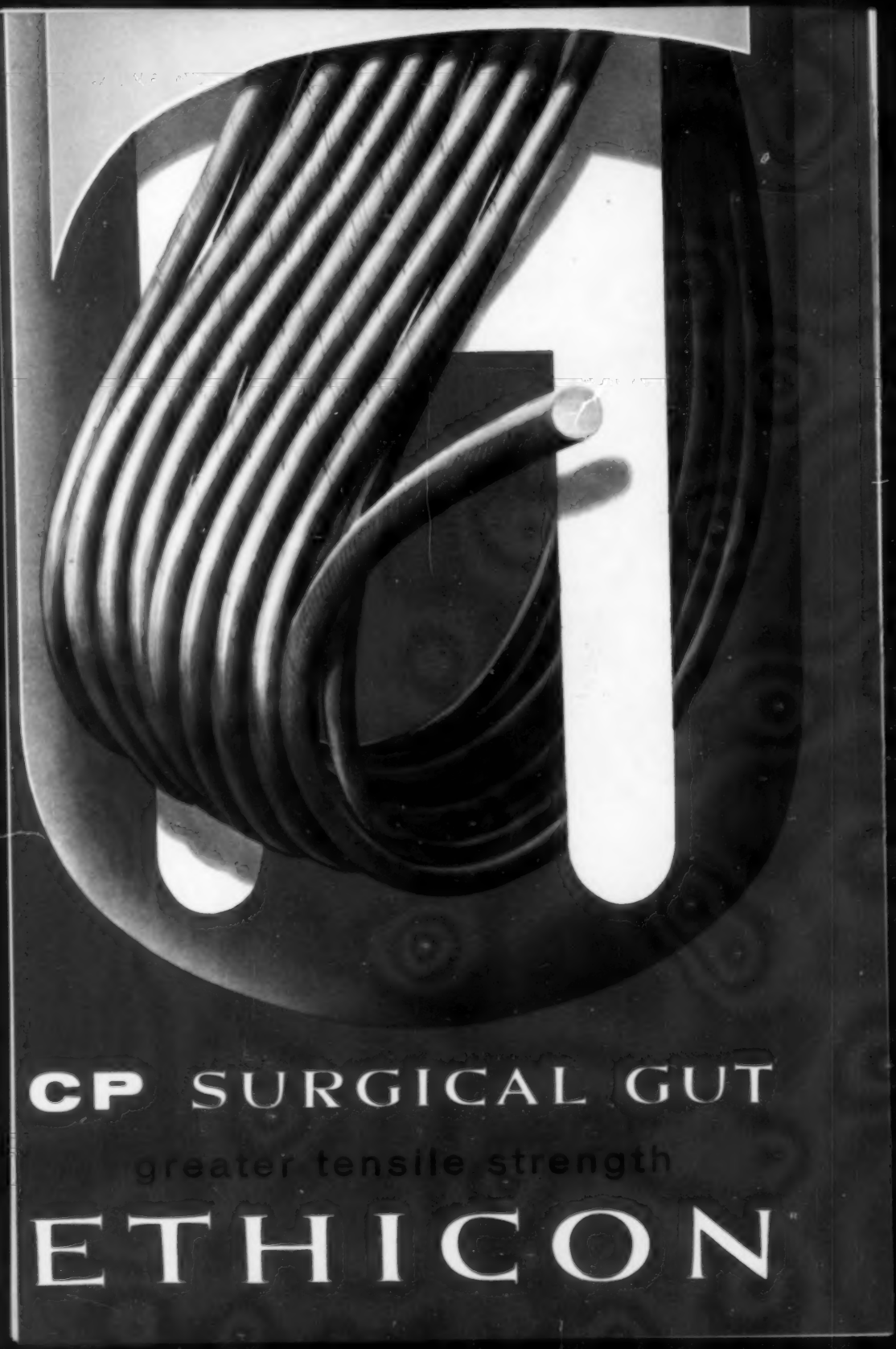
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Washington, D. C., November 2, 3 and 4, 1955

by

1. Shubin, H., and Heiken, C. A.
2. Morton, R. F.; LaCaille, R. A.; Gold, A., and Prigot, A.
3. Payne, H. M.; McKnight, H. V., and Harden, K. A.

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REFERENCES:

1. Camarata, S. J.; Jacobs, H. J., and Affeldt, J. E.: Read Before The Southern California Chapter of The American College of Surgeons, Palm Springs, Calif., January 23, 1953.
2. Miller, W. F.: New England J. Med. 251: 580, 1955.
3. Limber, C. R.; Reiser, H. G.; Roettig, L. C., and Curtis, G. M.: J.A.M.A. 149: 816, 1952.

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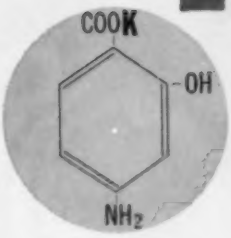

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1. *Molthan, L., Cohen, R. V., and Zarafonetis, C. J. D.: Clinical use of potassium para-aminosalicylate (KPAS). Am. Rev. of Tuberc. and Pulmon. Dis. 71:220 (Feb.) 1955.*

2. *Cohen, R. V., Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations). Read before the American Trudeau Society, Annual Meeting, Milwaukee, Wisconsin, May 23-27, 1955.*

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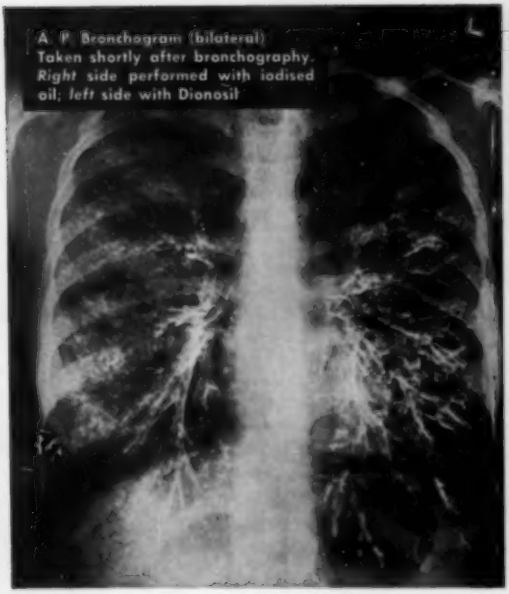
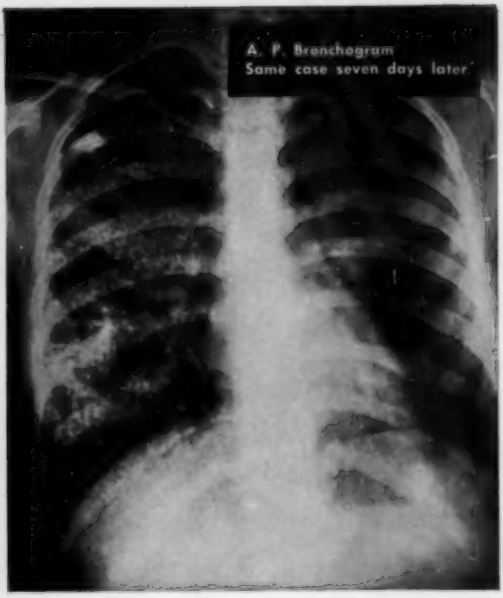

A. P. Bronchogram (bilateral)
Taken shortly after bronchography.
Right side performed with iodised oil; *left* side with Dionosil



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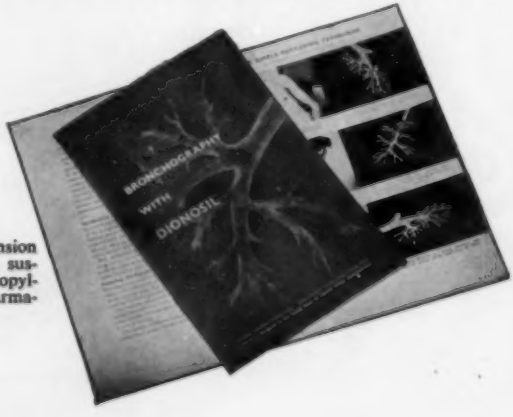

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New ganglionic blocker lowers blood pressure consistently, predictably, usually with just 2 oral doses per day

Patients with moderate to severe essential hypertension, and even with malignant hypertension, often respond satisfactorily to a ganglionic blocking agent such as Ecolid. It can be used alone or — for maximal control of blood pressure with minimal side effects — in combination with other antihypertensive agents such as Serpasil or Apresoline.

Advantages

Ecolid has the following advantages over other ganglionic blockers:

- long action, usually requires only two oral doses per day
- rapid absorption — promptly reduces systolic and diastolic pressures
- consistent and predictable response — smoother control
- lower dosage required than with other ganglionic blockers
- minimal likelihood of drug tolerance

Clinical observations

In a study of four ganglionic blocking agents, Winsor[1] found that the "most effective agent was SU3088 [Ecolid]...." In another comparative study, Grimson[2] reported: "Results with Ecolid have been definitely more encouraging than those with pentolinium." Patients maintained on Ecolid state that they prefer this ganglionic blocking agent because of greater energy, improved appetite, less difficulty with constipation and fewer tablets to take.[2,3]

For complete information about Ecolid, particularly more details on dosage recommendations, management of undesired effects and precautions, contact your CIBA representative or write to Medical Service Division for booklet entitled "Ecolid — A New Ganglionic Blocker for Hypertension."

References:

1. Winsor, T.: Am. J. M. Sc. *230*:133 (Aug.) 1955. 2. Grimson, K. S.: J.A.M.A. *158*:359 (June 4) 1955. 3. Grimson, K. S., Tarazi, A. K., and Fraser, J. W., Jr.: Circulation *11*:733 (May) 1955. 4. Grimson, K. S., Tarazi, A. K., and Fraser, J. W., Jr.: Angiology *6*:507 (Dec.) 1955. 5. Strawn, J. R., and Moyer, J. H.: Personal communication, 1955. 6. Maxwell, R. D. H., and Howie, T. J. G.: Brit. M. J. *2*:1189 (Nov. 12) 1955.

SUPPLIED: ECOLID Tablets (Rotocotes), 25 mg. (ivory) and 50 mg. (pink).

DOSAGE: Dosage must be adjusted to the individual patient. Below is a typical plan by which treatment may be initiated.

Ambulatory patients		
DAY	A.M.	P.M.
1	25 mg.	—
2	25 mg.	25 mg.
3	50 mg.	25 mg.
4	50 mg.	50 mg.
5	75 mg.	50 mg.
6	75 mg.	75 mg.
7	100 mg.	75 mg.
8	100 mg.	100 mg.

Hospitalized patients		
DAY	A.M.	P.M.
1	50 mg.	—
2	50 mg.	50 mg.
3	100 mg.	50 mg.
4	100 mg.	100 mg.

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REPRESENTATIVE CLINICAL STUDIES OF Ecolid*

Number of Patients	Initial Oral Dosage	Responses	Duration of Action	References
59 (Total Series)	75 to 300 mg. daily	Compared with other ganglionic blockers, small doses of Ecolid were employed and greater hypotensive effect was obtained. Rapid absorption and long duration of hypotensive action.	Postural hypotension lasted 13.4 hours in 5 "test" patients receiving doses of 150 mg.	1
20	50 to 200 mg. daily	Blood pressure in 20 well controlled; reductions lasted twice as long as those induced by pentolinium. Each of 10 patients with previous experience with hexamethonium preferred Ecolid. Less difficulty with constipation; appetite improved; greater energy.	**	2
18	50 to 100 mg. daily	Hypertension in 18 well controlled. Supine blood pressure reduced without tachycardia. Constipation occurred infrequently.	Supine blood pressure lowered for 12 hours or more with single oral doses of 50 to 100 mg.	3,4
44	50 mg. daily	35 responded well; 14 of these became normotensive. All patients received reserpine as base therapy.	**	5
12	25 to 200 mg. daily	Blood pressure of all 12 satisfactorily controlled. Systolic blood pressure lowered average of 76 mm. Diastolic blood pressure lowered average of 42 mm.	**	6

*To date, a total of 63 investigators have reported on the use of Ecolid in more than 500 patients. They were practically unanimous in the opinion that Ecolid was highly effective. Nearly all commented on the prolonged duration of action—about 8 to 12 hours—which permitted a twice daily dosage schedule in most cases.

**Information not available.

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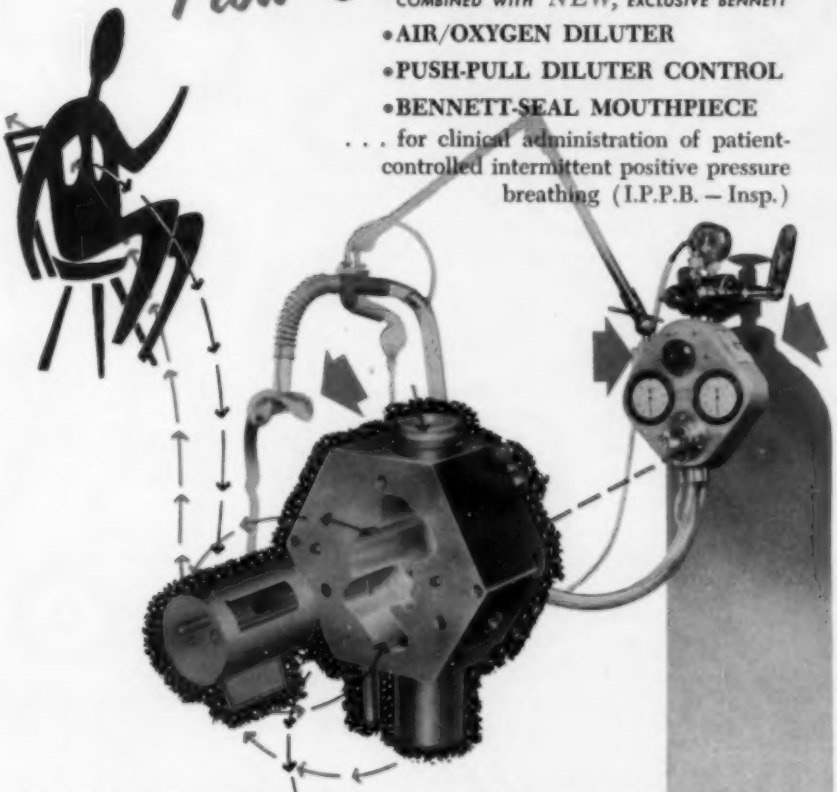

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DISEASES of the CHEST

VOLUME XXIX APRIL, 1956 NUMBER 4

"Gatalone" in the Treatment of Pulmonary Tuberculosis*

EUGENE J. DES AUTELS, M.D., F.C.C.P., KARL H. PFUETZE, M.D., F.C.C.P.
JAMES R. ZVETINA, M.D., CHARLOTTE A. COLWELL, Ph.D.
ADELINE R. HESS, M.S., and CLIFTON J. WOODS, M.S.

Hines, Illinois

Soon after a new compound d-glucuronolactone isonicotinyl hydrazone ("Gatalone"; INH-G) was synthesized by Passedouet et al[1] and independently by Sah,[2] the drug was reported to be highly active against tubercle bacilli and to be much less toxic than isoniazid on a weight for weight basis.[1, 3, 4, 5, 6] Early reports of its effectiveness in human tuberculosis seemed to justify further clinical trials.

This study was primarily planned to investigate the potential toxicity and anti-tuberculous activity of "Gatalone"** in the treatment of pulmonary tuberculosis. Simultaneously, the Bacteriology Section of the Research Service of this hospital undertook a study of the bacteriologic aspects including the emergence of bacterial resistance to the drug, cross resistance with isoniazid, and plasma concentrations of the drug.[7]

At the time this study was started, the authors were convinced isoniazid should not be given alone. Consequently, they did not randomize and concurrently treat a comparable group of patients with isoniazid alone.

Clinical Material

Eleven patients with pulmonary tuberculosis were selected for this study (Table I). All were male veterans ranging from 27 to 57 years of age. Eight of the 11 were less than 40 years of age. Six were white and five were Negro. Their weights ranged from 116 to 149 pounds (52.7 to 67.7 Kg.) at the start of treatment.

Before treatment, the chest roentgenograms of all cases were interpreted as consistent with a considerable component of exudative infiltration which was considered likely to respond to effective anti-tuberculous chemotherapy. The disease was far advanced in nine cases and moderately advanced in two. The lesions were bilateral in six and unilateral in five. Cavities were present in all. The diameter of the cavities were one centimeter in two and ranged from three to seven centimeters in nine.

The known duration of symptoms, before beginning treatment was less than six months in eight cases, nine months in one, and one year or more

*From the Tuberculosis and Research Services, Veterans Administration Hospital, Hines, Illinois.

**Generously supplied by Barnes-Hind, Inc., San Francisco, California.

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in two. No patient had previously received antimicrobial therapy for tuberculosis. None received any form of collapse therapy during the period of this study.

Treatment regimen: All patients were started on 400 mgms. of "Gatalone" four times daily by mouth and were continued on treatment for at least six months. However, the dosage was reduced to 1200 mgms. daily in two during the fifth (No. 3) and third (No. 11) months of treatment because of severe (No. 3) and moderate (No. 11) peripheral neuropathy. The dosage of 1600 mgms. of "Gatalone" contained the equivalent of approximately 732 mgms. of isoniazid, or 10.8 to 13.9 mgms. of isoniazid per kilogram of body weight daily.

Results of Treatment

Clinical response. Lessening of cough and expectoration, defervescence of fever, gain in weight and improvement of general condition was noted in all patients (Fig. 1). However, relapse of symptoms occurred during the fifth (No. 7) and sixth (No. 8) months of therapy in two cases. Cough was absent in two cases (No. 2 and No. 10) before treatment, disappeared in four, diminished to slight in three, and improved then worsened when relapse occurred in two (No. 7 and No. 8). The average quantity of expectoration diminished by two-thirds, but two patients (No. 7 and No. 8) again raised larger amounts upon relapse. Temperatures were between 100 and 103 degrees before treatment in nine cases, and subsided to normal in all (usually within two months); however, fever recurred in the two that relapsed. Two were afebrile before treatment and remained so. All gained weight ranging from five to 38 pounds (average 23.6 pounds).

Roentgenographic changes. At the end of six months of treatment x-ray films revealed marked improvement in three cases (Fig. 2), moderate im-

TABLE I
BACKGROUND FACTORS BEFORE "GATALONE" THERAPY IN ELEVEN CASES OF PULMONARY TUBERCULOSIS

Case No.	Age	Race	Dur. of Symptoms	General Condition	Stage of Disease	Cavity Size (Cm.)	Distrib. of Disease
1	36	W.	2 Yrs.	Fair	F.A.	L: 6.0	Unilat.
2	27	N.	Recent	Good	M.A.	L: 1.0	Unilat.
3	44	N.	2 Wks.	Fair	F.A.	L: 1.0	Unilat.
4	57	W.	1 Yr.	Fair	F.A.	L: 7.0	Bilat.
5	47	W.	2 Mos.	Fair	F.A.	L: 3.0	Bilat.
6	36	W.	5 Mos.	Poor	F.A.	L: 6.0	Bilat.
7	33	N.	3 Mos.	Fair	F.A.	R: 3.0	Bilat.
8	29	W.	Recent	Fair	F.A.	R: 3.0	Unilat.
9	33	N.	1 Mo.	Fair	F.A.	R: 4.0 L: 3.0	Unilat.
10	34	W.	6 Mos.	Good	M.A.	R: 3.0	Bilat.
11	39	N.	9 Mos.	Fair	F.A.	L: 5.0	Bilat.

provement in three, slight improvement in three, and worsening in two (No. 7 and No. 8) at the fifth and sixth months respectively (Fig. 3). Cavities were present in all cases before treatment but were lost to view in two cases (both one centimeter in diameter before treatment), reduced in size in four, remained unchanged in three, became larger in one (No. 7) and, in the remaining case (No. 5) the cavity became filled ("blocked").

Bacteriologic response. At the end of six months of treatment, repeated examinations of 24 hour sputum concentrates by smear failed to reveal tubercle bacilli in five of 11 cases. However, only three (Nos. 2, 5, 10) were negative by culture (three consecutive negative cultures), or a conversion rate of 27.3 per cent.

In summary, improvement in general conditions, decrease of cough and expectoration, defervescence of fever and gain in weight was reminiscent of improvement seen in patients who received isoniazid alone as their original course of anti-tuberculous chemotherapy. Moderate and marked roentgenographic improvement was observed in six of the 11 cases (54.5 per cent) and sputum conversion rate was 27.3 per cent. Two patients (No. 7 and No. 8) suffered clinical, roentgenologic and bacteriologic relapse.

Toxicity of Gatalone

Seven patients (63.6 per cent) complained of numbness and tingling of their hands and feet, usually late in the second month of therapy. These symptoms were mild in five cases, and were controlled by the administration of 300 to 450 mg. of vitamin B-6 daily. In two, moderate (No. 11) and severe (No. 3) symptoms were not controlled by vitamin B-6 until the dosage of "Gatalone" was reduced to 1200 mg. daily.

Four patients developed slight rash. There was no evidence of toxicity attributable to the renal, hepatic or hemopoietic system. Treatment was not discontinued because of drug toxicity in any case.

SUMMARY OF CLINICAL RESULTS IN ELEVEN CASES OF PULMONARY TUBERCULOSIS AT THE END OF SIX MONTHS OF TREATMENT WITH "GATALONE"

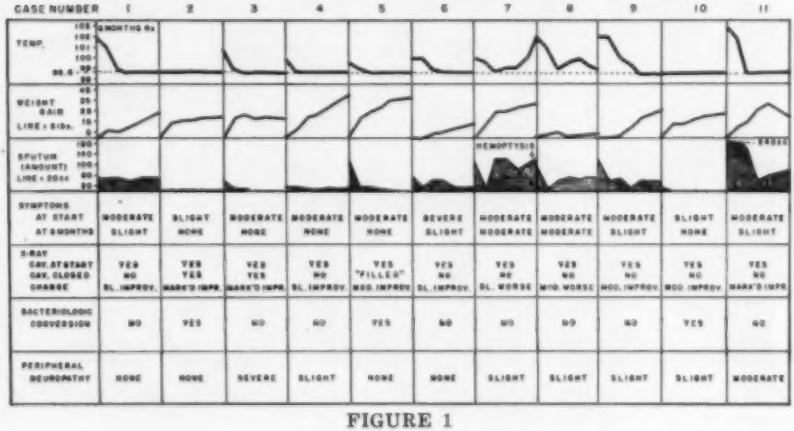

FIGURE 1

Discussion

This study was undertaken for the purpose of investigating the antituberculous effect and potential toxicity of "Gatalone." When comparing the effectiveness and toxicity of this drug with that of isoniazid, one must recall that approximately 45.76 per cent of the molecular weight of "Gatalone" is accounted for by the isoniazid portion of its chemical structure.[7] Other material factors are the comparative dosages per kilogram of body weight and the duration of treatment (or time period) at the time comparisons are made. There are valid objections to comparing our "Gatalone"-treated cases with those treated with isoniazid alone by other investigators at different times. Undoubtedly, there were differences in criteria for selection of cases, background factors, host factors, etc. Interpretations of serial roentgenograms and other elements may differ with different observers at the same time and the same observer at different times. However, when this study was started, the authors were convinced that isoniazid should not be used alone, and purposely refrained from randomizing and concurrently treating a comparable group of patients with isoniazid. Many informative reports concerning drug therapy of tuberculosis have likewise drawn comparisons between series of patients who were treated differently at different times by the same investigators, as well as at the same or different times by different investigators. Obviously, the comparison of results would be more valid were the patients selected according to strict criteria, randomized, and concurrently treated on the different drug regimens under comparison.

At the start of treatment, weights of the 11 patients ranged from 52.7 to 67.7 kilograms. The dosage of "Gatalone" was 1600 mgms. daily containing the equivalent of 732 mgms. of isoniazid, or 10.8 to 13.9 mgms.

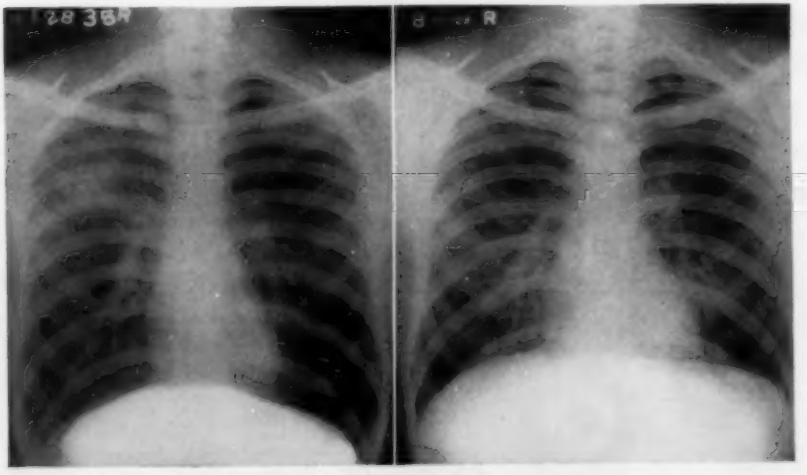

FIGURE 2—*Case 2:* (E. A.) Marked roentgenographic improvement at the end of six months of treatment with INH-G.

per kilogram of body weight. Since all patients gained weight there was some corresponding reduction in the dosage per kilogram of body weight during treatment.

Substantial (moderate and marked) roentgenographic improvement was observed in six of 11 patients (54.5 per cent) by the end of six months of treatment with "Gatalone." Within limits imposed by the small number of cases treated, this compares reasonably well with the incidence of substantial roentgenographic improvement reported in cases treated with 150 and 300 mgms. of isoniazid daily for five to eight months (38.0 per cent),[8] 28 weeks (50.6 per cent),[9] 28 weeks (43.1 per cent),[10] and in patients who completed six months of treatment on a dosage of 5.0 mgms. of isoniazid per kilogram of body weight daily (55.1 per cent).[14] (See Table II). Mount and his associates (USPHS Cooperative Study)[9, 10] found no statistically significant difference in the frequency of substantial roentgenographic improvement, whether isoniazid was given alone or in combination with 12.0 grams of PAS daily, or with one gram of streptomycin twice weekly. Mount and Ferebee[11, 12] again reported no statistically significant difference in the frequency of substantial roentgenographic improvement at 20 weeks[11] or at 32 weeks[12] between patients who received 3.0 and 10.0 mgms. of isoniazid per kilogram of body weight daily in combination with 12.0 gms. of PAS daily, or 1.0 gm. of streptomycin twice weekly; or when 10.0 mgms. of isoniazid per kg. of body weight was given concurrently with streptomycin plus PAS.

Thus, in the above reports and in this small series of "Gatalone"-treated cases there was little indication that higher dosages of isoniazid as such or in the form of "Gatalone," were more effective than 300 mgms. of isoniazid daily (in terms of substantial roentgenographic improvement); or that "Gatalone" had chemotherapeutic value aside from its content of isoniazid.

Since the dosage of "Gatalone" administered (1600 to 1200 mgms.) contained the equivalent of 732 to 549 mgms. of isoniazid, and since 150 mgms. of isoniazid seemed to be approximately as effective as higher dosages in the usual case of tuberculosis,[8, 9, 10, 11, 12] the authors could neither confirm

TABLE II
INCIDENCE OF SUBSTANTIAL ROENTGENOGRAPHIC IMPROVEMENT RELATED TO DOSAGES OF INH AND INH-G

Reference	Drug	Daily Dosage	Substantial X-ray Improvement Per Cent	Time-Period of Evaluation
V.A. SM Conf.[8]	INH	150 and 300 mgms.	38.0	5-8 Mos.
Mount et al[9]	INH	150-300 mgms.	50.6	28 Wks.
Mount et al[10]	INH	150-300 mgms.	43.1	28 Wks.
Deuschle et al[14]	INH	5 mg./Kg. body weight	55.1	6 Mos.
Present Authors	INH-G	1600 Mgms.*	54.5	6 Mos.

*Equivalent to 10.8 to 13.9 mgms. of isoniazid per kilogram of body weight daily.

nor deny the claim that weight for weight "Gatalone" was as effective as isoniazid. Concurrent treatment of two comparable groups of patients with 150 mgms. of "Gatalone" and with 150 mgms. of isoniazid might shed more light upon this point. *In-vitro* studies did not confirm the claim of equal effectiveness of the two drugs on a weight for weight basis but rather indicated that the activity of "Gatalone" depended primarily upon its content of isoniazid.[7]

Peripheral neuropathy developed in six of the 11 patients (54.5 per cent) by the third month and in seven (63.6 per cent) by the end of four months of treatment with 1600 mgms. of "Gatalone" daily (containing the equivalent of 10.8 to 13.9 mgms. of isoniazid per kilogram of body weight). Ferebee and Mount[11] reported peripheral neuropathy appeared in 3.4 per cent of a large group of patients who received 10 mgms. of isoniazid per kilogram of body weight daily for 12 weeks or longer. Deuschle et al[12] saw no instance of neuropathy among 32 patients who received five mgms. of isoniazid per kilogram of body weight daily for one year. Biehl et al[14, 15] noted evidence of peripheral neuropathy in 8 per cent, 18 per cent, and 44 per cent of their patients who received six to 10, 11 to 15, and 16 to 24 mgms. of isoniazid per kilogram of body weight daily. Hughes et al,[16] and Biehl and his associates[14, 15] found the incidence of peripheral neuritis was higher among those who excreted more free isoniazid and less acetylated isoniazid, especially among those who excreted substantial amounts of another unidentified breakdown product of isoniazid. They also found that the acetylated form of isoniazid was essentially inactive against tubercle bacilli. Demoen et al[17] reported that INH-G was largely excreted as such or as free INH, and that only a small fraction was excreted in acetylated form. The relatively high incidence of peripheral neuropathy

FIGURE 3—*Case 8:* (J. G.) Moderate roentgenographic worsening at the end of six months of treatment with INH-G.

among our patients may be explained on the basis of much less acetylation (detoxification) of INH-G due to the possible blocking action of D-glucuronolactone.[17] Among our patients treated with 1600 mgms. of INH-G daily (containing the equivalent of 10.8 to 13.9 mgms. of INH per kilogram of body weight), the incidence of peripheral neuropathy was actually higher (63.6 per cent) than the incidence reported by others (18 per cent)[14, 15] among patients treated on a dosage of 11 to 15 mgms. of INH per kilogram of body weight daily. However, the element of chance is relatively high in our small series of cases.

The authors believe "Gatalone" should be tried at lower dosages containing the equivalent of three to five mgms. of isoniazid (approximately six to 10 mgms. of "Gatalone") per kilogram of body weight daily. This dosage of "Gatalone" may contain sufficient isoniazid to be approximately as effective as higher dosages in the treatment of the usual case of pulmonary tuberculosis; and the incidence of toxicity might be considerably reduced. As is presently the general impression with isoniazid, it would seem consistent to recommend that, if possible, "Gatalone" should be used in combination with other anti-tuberculous drugs rather than alone.

If INH-G is predominately excreted in active forms INH-G and free isoniazid, rather than in the inactive acetylated form as is INH, it would seem desirable to investigate the possibility that INH-G may be more effective than INH in the treatment of renal and urologic tuberculosis.

SUMMARY

Eleven patients with pulmonary tuberculosis were treated with high dosages of "Gatalone" (usually 1600 mgms. daily) for a period of six months or longer.

At the end of six months of treatment symptomatic response was very favorable and substantial roentgenographic improvement was observed in six cases (54.5 per cent). The incidence of cavity closure was 27.3 per cent and the sputum conversion rate on three or more consecutive cultures was also 27.3 per cent.

Findings attributed to peripheral neuropathy appeared in seven patients (63.6 per cent). Whereas, weight for weight "Gatalone" may be less toxic than isoniazid, results in this small series suggest that isoniazid given in the form of "Gatalone" is no less toxic than isoniazid *per se* on a therapeutic dosage basis.

There was no indication that the higher dosages of isoniazid given in the form of "Gatalone" were more effective than 300 mgms. of isoniazid daily in the usual case of pulmonary tuberculosis; nor that "Gatalone" had chemotherapy virtue aside from its content of isoniazid.

SUMARIO

Once pacientes con tuberculosis pulmonar fueron tratados con altas dosis de "Gatalone." La dosis generalmente administrada fue de 1600 milígramos por día por un período de no menos de seis meses.

Al cabo de seis meses de tratamiento, la respuesta sintomática fué muy favorable y se notó una mejoría sintomatológica y radiográfica en seis de

los casos (54.5%). También se observó el colapso de las cavidades en 27.3% de los casos. La desaparición de bacilos en trés o más cultivos fué observada en 27.3% de los casos.

En siete pacientes (63.6%) se observaron trastornos neuropáticos periféricos. Aunque "Gatalone" es quizás menos tóxica que la isoniacida en iguales dosis, los resultados obtenidos en esta pequeña serie nos hace creer que la isoniacida administrada en la forma de "Gatalone" no es menos tóxica que la isoniacida propia, si se compara desde el punto de vista de dosis.

No se puede concluir que la "Gatalone" en las dosis administradas fué mas efectiva que 300 mgs. de isoniacida par día en los casos corrientes de tuberculosis pulmonar, ni tampoco se ha podido cerciorar que "Gatalone" tiene poderes terapéuticos otros que los debido a su contenido en isoniacida.

RESUME

Onze malades atteints de tuberculose pulmonaire furent traités par de hautes doses de "gatalone" (généralement 1.600 mmgr. par jour) pendant une période de six mois ou davantage.

A la fin de ces six mois, les symptômes s'améliorèrent beaucoup et des progrès radiologiques marqués furent observés dans six cas (54,5%). La fréquence de la fermeture des cavités fut de 27,3% et le pourcentage de négativations des crachats sur trois cultures ou davantage fut également de 27,3%.

Des constatations attribuées à une atteinte nerveuse périphérique apparurent chez 7 malades (63,6%). Bien qu'à poids égal, le "gatalone" peut être moins toxique que l'isoniazide, les résultats que les auteurs ont obtenus dans leur petite série font penser que l'isoniazide donné sous forme de "gatalone" n'est pas moins toxique que l'isoniazide lui-même si on tient compete d'unités pondérales équivalentes.

Les auteurs n'ont pas eu l'occasion de remarquer que de plus hautes doses d'isoniazide données sous forme de gatalone seraient plus efficaces que les 300 mmgr. d'isoniazide quotidiennement administrés dans les cas habituels de tuberculose pulmonaire. Ils n'ont pas noté non plus que le "gatalone" ait une vertu chimiothérapique propre en dehors de celle de l'isoniazide qu'il renferme.

ZUSAMMENFASSUNG

11 Patienten wurden mit hohen Dosierungen von "Gatalon" (gewöhnlich 1600 mgr täglich) während eines Zeitraumes von sechs Monaten und länger behandelt.

Am Ende der sechs Behandlungsmonate war der symptomatische Erfolg sehr günstig, und in 6 Fällen (54,5%) wurde eine greifbare röntgenologische Besserung beobachtet. Zum Kavernenschluss kam es in 27,3% der Fälle, und die Sputum-Konversion betrug nach drei oder mehr aufeinanderfolgenden Kulturen ebenfalls 27,3%.

Befunde, die der peripheren Neuropathie zuzuschreiben waren, traten bei 7 Patienten (63,6%) auf. Demgegenüber mag eine der Isoniazid-Dosierung entsprechende Medikation von "Gatalon" weniger toxisch sein als reines Isoniazid. Die Ergebnisse dieser kleinen Versuchsserie lassen

vermuten, dass Isoniazid, in Form von "Gatalon" verabreicht, nicht weniger toxisch ist als Isoniazid in therapeutischer Dosierung.

Es zeigte sich, dass die höhere Dosierung des Isoniazid im "Gatalon" nicht wirksamer war als die tägliche Gabe von 300 mgr Isoniazid, die bei der gewöhnlichen Lungentuberkulose erforderlich ist; ausserdem zeigte sich, dass die Wirksamkeit des "Gatalon" lediglich auf seinem Isoniazid-Anteil beruht.

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Pheochromocytoma, Factors in the Accurate Pharmacologic Diagnosis*

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Pheochromocytoma or the tumor of the medullary portion of the adrenal gland is a challenge to the clinician, investigator, biochemist, surgeon and pathologist. Although intrathoracic pheochromocytomas are rare, it is important that the chest physician and chest surgeon should be aware of the hazards of such tumors. The correct preoperative diagnosis of pheochromocytoma can be a lifesaving measure.

An estimated 90 per cent of pheochromocytomas arise from the adrenal medulla, but they may occur along the entire length of the sympathetic nervous system, that is wherever chromaffin tissue is found in the ganglia of the cervical, thoracic and abdominal sympathetic chains. In addition pheochromocytomas have been found in the organ of Zuckerkandl located on either side of the aorta at the origin of the inferior mesenteric artery.

Only four intrathoracic tumors have been reported in the literature and two were successfully removed. The first two were noted at necropsy; the first was found by Miller[1] in 1924 in the right costovertebral region at the level of the sixth rib. The second, reported by Philips[2] in 1940, was found at the apex of the left pleural cavity and probably arose from the first left thoracic ganglion. In the third case the diagnosis was made preoperatively for the first time and the tumor was successfully removed. This case was reported in 1949 by Maier.[3] Pheochromocytoma was suspected because the patient had an unexplained hypertension and an intrathoracic tumor near the sympathetic chain in the costovertebral region. Because of this, blood pressure readings were made at intervals of five minutes during the operation and epinephrine (adrenalin) was ready for immediate use. Care was taken to minimize manipulation of the tumor during the freeing of the mass in order to avoid hypertensive crisis. Within five minutes after the blood vessels leading to the tumor were clamped, the systolic blood pressure dropped from 210 to 110 mm. of mercury and a few minutes later was barely obtainable. Adrenalin was given intravenously and the blood pressure rose gradually and remained normal throughout the first postoperative day. The patient is still in good health.

In the fourth case, reported in 1950 by Overholt,[4] the diagnosis of pheochromocytoma was not suspected until operation. A lesion in the chest was noted on routine examination. The blood pressure was normal and

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the only significant symptom was a definite history of mild intolerance to heat. A diagnosis of posterior mediastinal neurofibroma was made, and the patient was prepared for operation. When the patient was placed on the operating table, the blood pressure was found to be 240/160 mm. of mercury, and the pulse rate, 160 beats per minute. The systolic blood pressure shortly rose to 270 and a pheochromocytoma was suspected. The tumor was lying half on the fourth, fifth, sixth and seventh vertebral bodies and half on the heads of the adjacent ribs. It was in line with the sympathetic chain which could be seen to disappear into it from above and emerge from it below. The vascular supply of the tumor was divided, and when the interruption of the supply was completed, a precipitous fall in blood pressure occurred to 90/70 mm. of mercury. At this time, blood was pumped rapidly into the vein and five minims of phenylephrine hydrochloride (neosynephrine) was given intravenously. An additional three minims of neosynephrine was given with an elevation of the systolic blood pressure to 100 mm. for the duration of the closure; however, when the patient was returned to bed, the blood pressure fell to 40 mm. of mercury systolic and neosynephrine was again given with effect. Today this patient is well.

Pertinent information, in addition to that on primary lesions in the chest, may be obtained from routine x-ray examination of the chest and physical examination about the neck. In one of our patients who had a pheochromocytoma primary in the left adrenal, a lesion was noted in the right seventh rib in the routine roentgenogram of the thorax. This was later found to be a metastatic lesion from the tumor in the adrenal. A second patient had an enlarged node in the left supraclavicular region five months after removal of a tumor from the hilus of the liver behind the common bile duct and foramen of Winslow. A histamine test gave a negative result 10 days after removal of the hilar tumor, but was positive five months later. After removal of the node from low in the deep cervical chain, the histamine test again gave negative results. Because the histamine test was positive for pheochromocytoma before both operations, the usual preparations were made for the operations. Both of these patients have returned with further metastasis.

Bartels and Cattell[5] have reported a similar case. Their patient remained well for a year after the removal of a tumor from the left adrenal, and then swelling developed in the right side of the neck. Biopsy revealed this to be a metastatic pheochromocytoma.

A sudden hypertensive reaction during any operative procedure should cause the surgeon to suspect pheochromocytoma. Today the antiadrenergic drugs are available to combat the hypertension resulting from these tumors during operation, and phenylephrine hydrochloride (neosynephrine) and norepinephrine (arterenol) are available to restore the blood pressure to normal levels after the removal of the tumors.

Pheochromocytoma may be associated with sustained hypertension or with paroxysmal hypertension associated with attacks similar to those following the administration of large amounts of epinephrine or norepineph-

rine. Thus any patient who has a paravertebral tumor in the thorax and gives a history of paroxysmal hypertension associated with tachycardia, headache, intolerance to heat, excessive sweating and sometimes nausea and vomiting should be suspected of having a pheochromocytoma. Likewise a patient with a tumor in the thorax and sustained hypertension with or without these same symptoms may also be suspected of having pheochromocytoma, particularly if the history of hypertension has been short.

In order to establish a correct diagnosis before operation, there are simple pharmacologic tests which can be carried out by a physician in a short period.

The Pharmacologic Tests[6-12]

In cases of paroxysmal hypertension due to pheochromocytoma, administration of histamine, tetraethylammonium chloride (TEAC) and metha-

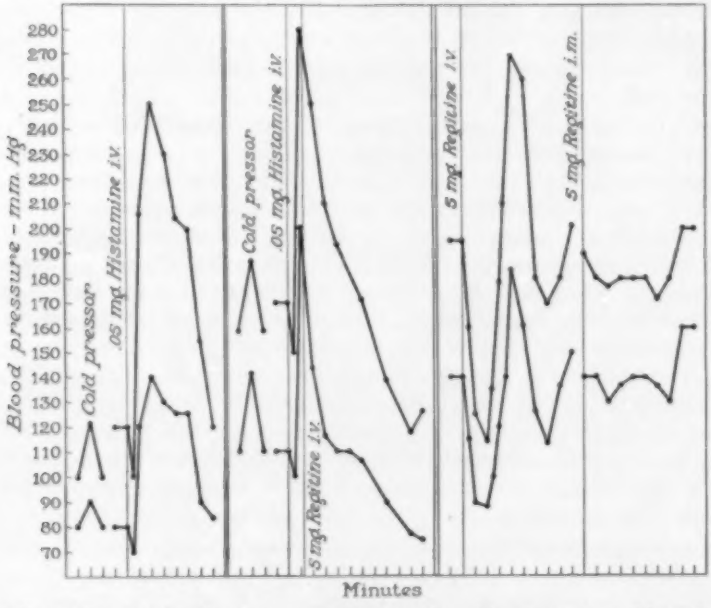

FIGURE 1: Changes in blood pressure during the cold pressor test, histamine test and regitine test. *Left.* The rise in blood pressure during the immersion of one hand in cold water at 4° C. for 1 minute and after the intravenous administration of 0.05 mg. of histamine base in 0.5 cc. of physiologic solution of sodium chloride should be noted. Thirty seconds after the injection of histamine the blood pressure fell and 2 minutes later rose precipitously. These observations indicate a pheochromocytoma. *Center.* The rise in blood pressure during the cold pressor test and the more precipitous rise following the injection of histamine should be noted. At the height of the response to histamine which was due to the release of the pressor amines, regitine, given intravenously, produced a precipitous fall in blood pressure together with a cessation of all clinical signs and symptoms; thus two tests were positive for pheochromocytoma. *Right.* The sudden rapid fall of the blood pressure after the intravenous injection of 5 mg. of regitine is interpreted as a positive result indicative of pheochromocytoma. Practically no fall but instead a rise in the blood pressure followed intramuscular administration of 5 mg. of regitine. This indicates that a pheochromocytoma is not present. This was a false negative result in this case.

choline chloride (mecholyl) stimulates the discharge of the pressor substances from the tumor and produces characteristic attacks similar to those that occur spontaneously. In cases of sustained hypertension, phentolamine (regitine) and piperoxan lower the blood pressure by blocking the pressor effect of epinephrine and norepinephrine in the blood if a pheochromocytoma is present. In the pharmacologic test with these drugs, one is dependent on a precipitous fall in blood pressure for the demonstration of the circulating pressor substances.

Although we have used all these drugs as they were introduced, we have more frequently used histamine for patients with paroxysmal hypertension and regitine for the patients with sustained hypertension. At this time, we should like to discuss all the precautions concerned with these tests.

The cold pressor test is an integral part of the histamine test as the rise of the blood pressure during the cold pressor test measures the lability of the blood pressure and is the measuring stick for the response of the blood pressure two minutes after the intravenous injection of histamine (Fig. 1). For the histamine test as we carry it out, histamine is never given as an infusion; 0.05 mg. of histamine base in 0.5 cc. of normal saline solution is placed in a tuberculin syringe and is injected intravenously. The blood pressure always falls 30 seconds after the injection or the histamine did not enter the vein. Immediately thereafter the blood pressure rises rapidly, and the characteristic clinical signs and symptoms of a severe episode appear. In any one patient, one or more of the characteristic symptoms of the episode may be lacking.

For the result of a test with histamine in the patient with normal levels of blood pressure between attacks to be interpreted as positive for pheochromocytoma, the rise in blood pressure two minutes after the injection should be at least 60 mm. systolic and 40 mm. diastolic. The average rise for 19 patients with pheochromocytoma was 106 mm. systolic and 56 mm. diastolic. This was an average of 70 mm. systolic and 19 mm. diastolic above the average response of the blood pressure during the cold pressor test.

The histamine test is used for patients with paroxysmal hypertension but not for sustained hypertension. Usually when there is sustained hypertension with a basal blood pressure of more than 170/110, regitine is used. For the patient with mild persistent hypertension and a history of paroxysmal attacks, with a basal blood pressure of less than 170/110, both histamine and regitine are used as follows: The needle is left in the vein following the administration of histamine and another syringe containing regitine is attached. The blood pressure is determined repeatedly for two minutes after the injection of histamine, then regitine is injected. If the rise in blood pressure after the injection of histamine is due to the pressor amines from a pheochromocytoma, all symptoms will disappear and the blood pressure will fall in 30 to 60 seconds after injection of regitine. Therefore, histamine may be given with safety and two positive

tests will be obtained (Fig. 1). If the patient has mild essential hypertension, the blood pressure will not rise as high when histamine is given as it will if the patient has a pheochromocytoma, and after the administration of regitine the headache will not disappear and the blood pressure will not fall rapidly. If regitine is given alone to such a patient between paroxysms, the blood pressure may rise instead of fall in the presence of a tumor as there will be no pressor amine in the blood to cause the precipitous fall in blood pressure between attacks.

To the patient with sustained hypertension, 5 mg. of regitine is administered intravenously, not intramuscularly for the test. As you will note in Figure 1, a negative result may be obtained when regitine is given intramuscularly in the presence of a tumor. Regitine rather than piperoxan is used for the first test on patients with sustained hypertension as there are fewer side reactions with regitine and no hazardous pressor responses when the patient has essential hypertension. True, regitine has

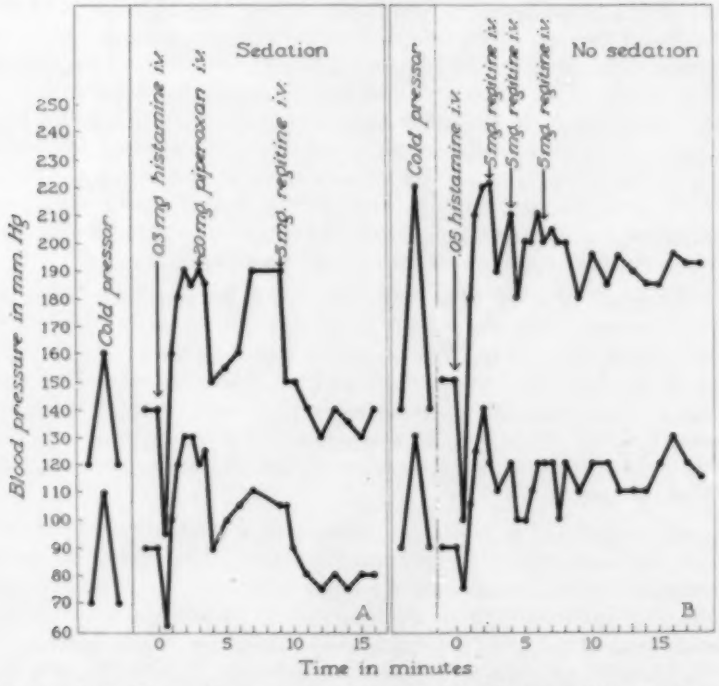

FIGURE 2: *Left.* Observations made during sedation. The rise of the blood pressure was less during the cold pressor test than 2 minutes after the injection of histamine and the fall of the blood pressure following administration of piperoxan and regitine was sufficiently great to indicate the presence of a pheochromocytoma. *Right.* Observations made after sedation had been discontinued for 48 hours in the same patient. The rise of the blood pressure was greater during the cold pressor test than 2 minutes after the injection of histamine. Likewise, when three times as much regitine was given, the fall in blood pressure was considerably less than during sedation. The histamine and regitine tests indicate absence of pheochromocytoma. This patient was operated on and no tumors were found.

a greater tendency to cause a fall in the blood pressure during the first minute when no pheochromocytoma is present, but the blood pressure returns in the next minute to a level which will be considered negative for pheochromocytoma.

Before any of these tests are carried out, the use of any sedative or narcotic should be prohibited for 48 hours and possible self-medication should be checked as the pharmacologic tests may yield false positive results under these conditions. First, sedatives inhibit the rise of the blood pressure during the cold pressor test which is the measuring stick. The effect of sedation is demonstrated in Figure 2. In a case of paroxysmal hypertension, histamine produced a rise greater than the cold pressor test during sedation, thus indicating the presence of a tumor. Both piperoxan and regitine produced a marked fall during sedation. However, when the sedation was discontinued for 48 hours, the two minute rise with histamine was less than that of the cold pressor test and three times as much regitine as given during sedation did not produce the previous fall in blood pressure. No tumor was found at operation.

In a patient with sustained hypertension, barbiturates, meperidine hydrochloride (demerol), morphine, chloral hydrate and probably many other sedatives produce a fall in blood pressure following intravenous administration of regitine or piperoxan typical of that produced by a tumor. Shock seems greater in the patient who has had sedation and no tumor than in the patient with pheochromocytoma and no sedation, although the fall in blood pressure may be the same. The false positive result during sedation and the negative result after discontinuation of sedation are indicated in Figure 3. The fact that a false positive result is obtained during sedation has been proved by operation as no tumors were found. When a patient has a severely elevated blood pressure, it is always logical to hospitalize and to sedate him. Subsequently, while he is in the hospital and under sedation, the pharmacologic tests are carried out and a false positive result is obtained which would indicate the presence of a tumor.

It is a good idea when screening patients for pheochromocytoma to measure the blood pressure on both arms because a difference in blood pressure of from 10 to 80 mm. of mercury systolic has been found in the two arms of the same patient. Two cases will be cited briefly to demonstrate how a false positive diagnosis may be obtained during the pharmacologic tests.

In the first patient a histamine test and a cold pressor test were carried out first on the right arm and subsequently on the left arm. The basal blood pressure in the two arms varied by 52 mm. systolic and 38 mm. diastolic. The blood pressure on the cold pressor test rose approximately the same amount in both arms. In order to have a positive result from the histamine test on the right side the blood pressure should rise considerably higher than it did during the cold pressor test on that same side. If the blood pressure is not measured simultaneously in both arms or is measured in one arm for the cold pressor test and in the other arm when

the histamine is given, a false positive result could be obtained. By measuring the blood pressure simultaneously in both arms the reaction to histamine was found to be negative.

The second patient was sent to us with a diagnosis of pheochromocytoma. The basal blood pressure varied greatly in the two arms. When the blood pressure is measured on the arm with the highest pressure after the intravenous injection of regitine or piperoxan, the blood pressure may fall to the level of the opposite arm, which in this case was a fall of 80 mm. systolic and 40 mm. diastolic. This could easily be interpreted as a positive response. When the blood pressures were determined simultaneously in the two arms, there was little or no fall in the blood pressure on either arm following the intravenous injection of 5 mg. of regitine. If a tumor were present, a pronounced fall would have occurred on both sides. Therefore, the blood pressure is measured routinely on both arms of all patients and if there is any disparity, blood pressures are determined simultaneously in both arms during the pharmacologic tests.

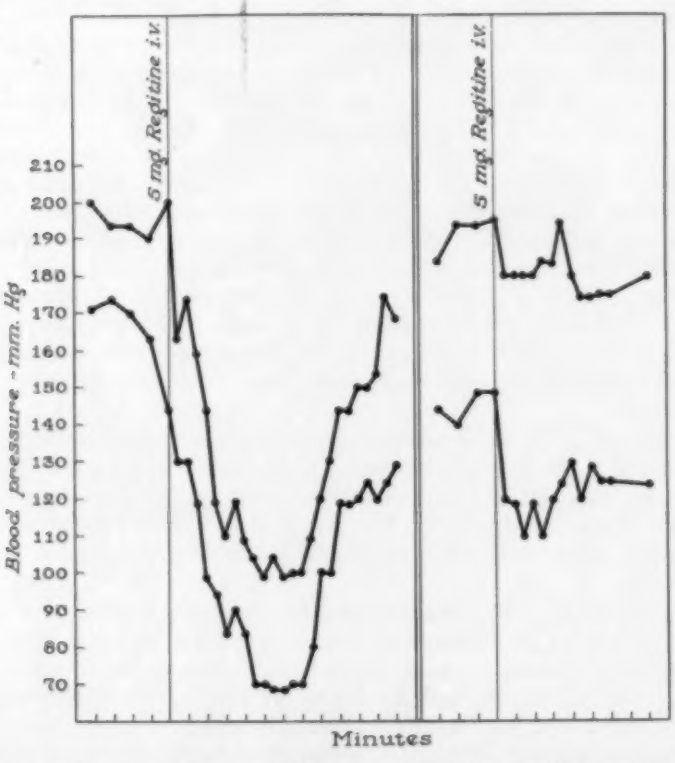

FIGURE 3: *Left.* Observations made during sedation. The precipitous fall in blood pressure of a patient with hypertension seems to indicate the presence of a pheochromocytoma. *Right.* Observations 5 days after sedation had been discontinued. The slight fall in blood pressure should be noted. No tumor was found at operation.

With the introduction of the antihypertensive drugs, another difficulty has arisen, namely false negative results (Fig. 4). In two cases in which a tumor was found at operation, the first had two negative tests followed by a positive test when use of hydralazine (apresoline) was discontinued; in the second case we obtained an equivocal result from the test until use of the drug was discontinued for 8 days. This situation is difficult to deal with because we do not know how long administration of these drugs must be discontinued but apparently for some time. Sometimes, because the sweating disappears when hydralazine (apresoline) is given, the return of sweating may be an indication of the time when a clear-cut test can be obtained. At present we are not able to state definitely the effect of the Rauwolfia compounds on the pharmacologic tests.

By close observation of these various difficulties during the past 10 years, we have carried out 7,500 pharmacologic tests on 6,061 patients, and we have found 55 pheochromocytomas in 45 patients. The diagnosis has been proved correct at operation.

No deaths or untoward effects have occurred in any of these patients during the tests before operation, during operation or immediately after operation. This has been largely due to extremely close and careful observation of the patient during and after operation. In all patients now a transverse abdominal incision[13] is made in order that all tumor-

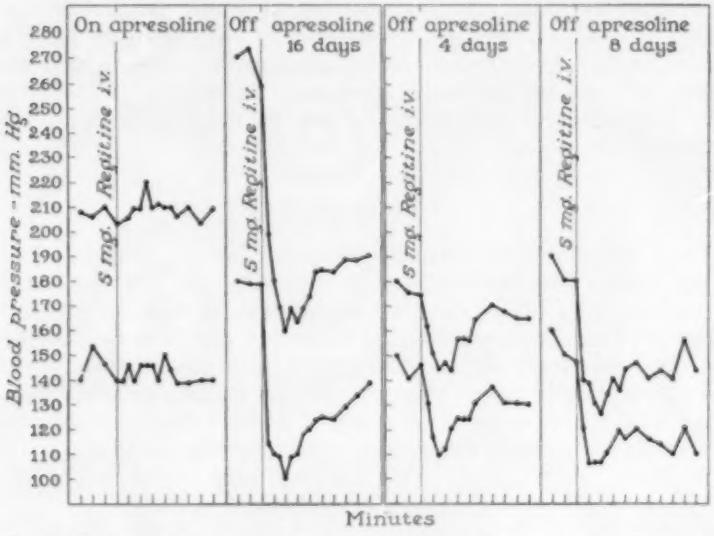

FIGURE 4: The blood pressure after the intravenous injection of regitine while the patient was receiving antihypertensive drug, apresoline, should be noted. After administration of apresoline was discontinued for 16 days, a precipitous fall of blood pressure occurred after the injection of regitine. This indicates a pheochromocytoma and the tumor was found at operation. Note the equivocal fall of the blood pressure after the injection of regitine after administration of apresoline had been stopped for 4 days. After administration of apresoline had been discontinued for 8 days, a more precipitous fall in blood pressure occurred after the injection of regitine. This indicates a pheochromocytoma, and, as said before, one was found at operation.

bearing regions may be explored. We have determined the blood pressure at intervals of one minute during the operation. Thus, when pronounced hypertensive effects occur, regitine is given immediately to lower the blood pressure and when removal of the tumor is accompanied by a sharp fall in the blood pressure, norepinephrine is administered. After a tumor is removed, a sudden rapid rise in the blood pressure which is maintained indicates the presence of another tumor.

SUMMARY

The precautions which are necessary to procure a successful pharmacologic test for pheochromocytoma have been discussed. These tests with the proper precautions can be carried out quickly and without hazard. A preoperative diagnosis of pheochromocytoma in any patient with hypertension and a tumor located paravertebrally in the chest can be made by these pharmacologic tests. Thus, fatalities or untoward reactions may be avoided during operation because of an unexpected pheochromocytoma.

RESUMEN

Se discuten las precauciones necesarias para llevar a cabo una prueba farmacológica con éxito en el feocromocitoma. Estas pruebas con las precauciones adecuadas pueden realizarse pronto y sin pelgiro. Se puede hacer un diagnóstico preoperatorio de feocromocitoma en cualquier enfermo con hipertensión y tumor localizado paravertebralmente en el tórax. Puede evitarse la mortalidad durante las operaciones a causa de un feocromocitoma inesperado.

RESUME

L'auteur discute les précautions nécessaires pour l'obtention d'un test pharmacologique satisfaisant pour le diagnostic de phéochromocytome. Ces examens avec les précautions nécessaires peuvent être poursuivis rapidement et sans danger. Un diagnostic préopératoire de phéochromocytome chez chaque malade atteint d'hypertension et de tumeur paravertébrale localisée dans le thorax, peut être fait par les tests pharmacologiques. C'est pourquoi les erreurs et les réactions douteuses dues à un phéochromocytome inattendu peuvent être évitées pendant l'opération.

ZUSAMMENFASSUNG

Die zur erfolgreichen Durchführung eines pharmakologischen Testes auf Phaeochromozytom notwendigen Kautelen wurden besprochen. Diese Tests können unter Berücksichtigung der richtigen Vorsichtsmassnahmen schnell und ohne Risiko ausgeführt werden. Durch diese pharmakologischen Tests kann bei jedem Patienten mit Hypertonie und paravertebralem intrapulmonalem Tumor die Diagnose eines Phaeochromozytoms

gestellt werden. Hierdurch können Todesfälle und unerwünschte Reaktionen während der Operation durch das unerwartete Vorhandensein eines Phaechromozytoms vermieden werden.

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Displacements of the Barium-Filled Esophagus by Cardiovascular Lesions*

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The close anatomic relationship of the esophagus to the heart and aorta permits of important diagnostic observations concerning many cardiovascular lesions. Two other characteristics of the esophagus make such studies of practical significance. This elongated, soft and hollow tube responds readily to external pressure, and it is easily visualized following the ingestion of a barium paste. Valuable information concerning various cardiovascular abnormalities can thus be gained from pressure defects or displacements which frequently result from lesions of the neighboring heart and aorta.

Anatomy

The esophagus enters and passes through the thorax as a fairly straight tube (Fig. 1). It has a slight posterior curve to conform somewhat to the aorta to which it is intimately bound by fibrous tissue. It lies anteriorly to the aorta, and maintains a distance of 1 to 3 cm. between its posterior wall and the anterior surface of the spine. In the right lateral position, the esophagus is seen to bisect the normal chest.

The *anterior wall* of the esophagus may present the following indentations noted from above downward: a) the aortic arch impression in its upper third, b) a shallower indentation below this produced by the pulmonary artery and large bronchi, c) and from this point down to a point 2 cm. above the diaphragm, a distance of 6 cm., it lies in close contact with the left auricle. It then curves anteriorly just above the diaphragm to enter the abdominal cavity through the esophageal hiatus.

The *posterior wall* of the esophagus is in intimate contact with the arch ("bed of the aorta") and descending aorta. Because of the periaortic fibrous tissue, it follows the descending aorta closely throughout its extent and, therefore, is affected by any deviation or lesion of this vascular structure. Although it remains to the right of the descending aorta throughout its course in the thorax, it crosses this vessel to pass sharply to the left, just above the diaphragm.

Method of Examination

A very thick barium paste is prepared. The patient is instructed to swallow it after roentgenoscopic or fluoroscopic preparations are completed. X-ray films are exposed a moment or two later during inspiration. The following positions are most important: posteroanterior (PA), right

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anterior oblique (RAO), left anterior oblique (LAO), and right lateral (RL). The left auricle is best visualized in the RAO, PA and RL views. The aortic arch can be measured in the PA view. The descending aorta is studied in the LAO and PA positions.

Congenital Anomalies

Although the following anomalies are not common, they may produce symptoms and findings of esophageal or tracheal compression. Anomalies which produce vascular rings completely envelop both structures. They include double aortic arch and right aortic arch. The latter completes the ring by its attachment to the pulmonary artery by a short ligamentum arteriosus or patent ductus.

1. *Anomalous Right Subclavian Artery*

This aberrant vessel arises from the left side of the arch or from the left subclavian artery. In order to supply the right arm, it must cross to the right behind the esophagus, usually at the level of the third dorsal vertebra. More rarely, it passes in front of the esophagus or trachea. During infancy, it may produce hesitancy in swallowing (dysphagia lusoria).

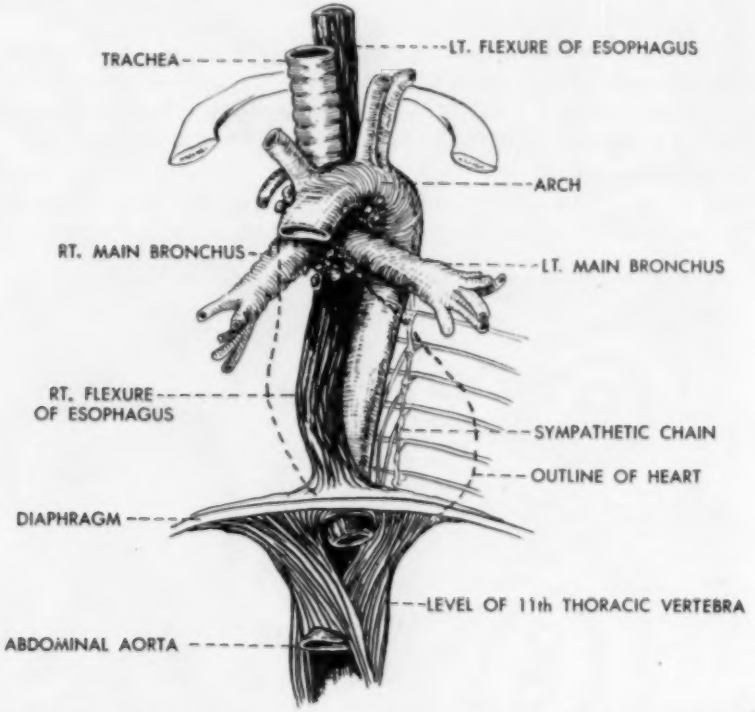

FIGURE 1: Relationship of cardiovascular structures to the esophagus (from Reich, N. E.: Diseases of the Aorta, N. Y., MacMillan Co., 1949).

Symptoms may also appear in later years, owing to arteriosclerosis or dilatation of the vessel which produces compression.

X-ray films reveal a localized compression of the barium column in an oblique direction at the level of the third vertebra and above the aortic arch (Fig. 2). This can be corroborated with angiocardiographic studies or aortography.

2. *Right Aortic Arch*

An abnormal persistence of the right fourth branchial artery with a disappearance of its left counterpart results in this anomaly. The aorta arises normally but ascends towards the right and courses toward the left behind the esophagus. It continues downward slightly to the right of the normal position. This condition is asymptomatic. A right aortic arch is also present in one-fourth of all cases of tetralogy of Fallot.

X-ray studies of the barium-filled esophagus reveal a characteristic compression: a) from the right, and b) from behind, displacing this structure to the left and forward at the level of the third or fourth thoracic vertebra (Figs. 3 and 4). The right aortic arch may sometimes form a constricting vascular ring by its connection to the right pulmonary artery through a patent ductus arteriosus or ligamentum arteriosus. Since the effects are similar, the condition will be discussed under double aortic arch.

3. *Right Aortic Arch with Left Descending Aorta*

This congenital lesion produces a distinct change in the course of the esophagus since the descending portion of the aorta crosses behind the esophagus, displacing it anteriorly. Oblique x-ray views clearly demonstrate the barium-filled esophagus in front of the great vessels.

4. *Right Descending Aorta*

This anomaly is almost always found in conjunction with a right aortic arch, but it also has recently been described as a continuation from a left

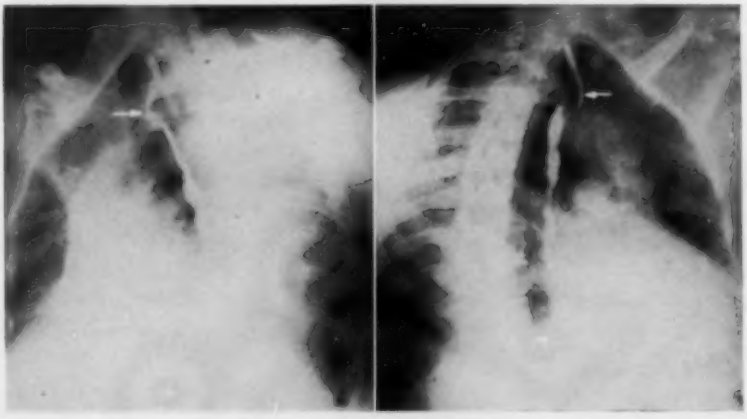

FIGURE 2: *Anomalous Right Sub-clavian Artery.* White male of 59 years, asymptomatic. *LAO and RAO Views*: Localized forward bulge of the esophagus just above the aortic arch.

aortic arch.[2] In such instances, the descending portion proceeds downward to the right of the vertebral column.

X-ray films are informative since the common adhesions of the esophagus and the aorta cause both structures to become displaced simultaneously. The aorta may be deviated well to the right of its normal position throughout its entire course (Fig. 5).

5. *Double Aortic Arch*

A bifid arch occurs when both fourth branchial arteries persist. The left (anterior) branch is almost always smaller than the right. When the vascular ring is small, the encircled esophagus and trachea are compressed. Dysphagia with esophageal dilatation and ulceration may appear above the point of compression.

Fluoroscopy shows hesitation of the barium column for a considerable period of time at the point of constriction, and barium is regurgitated in small quantities (dysphagia lusoria). X-ray films (Fig. 6) show a bilateral compression of the esophagus.[3] Lipiodol studies and angiocardiography (7 second film) offer corroborative evidence of the annular constriction produced by the vascular ring.

6. *Truncus Arteriosus*

A single abnormally wide vessel arising from the heart which provides the functions of an aorta and pulmonary artery is termed truncus arteriosus. This results from a failure of development of the aortic septum. Therefore, the single vessel must override both ventricles. There may be cyanosis of varying degree and clubbing. The heart is greatly enlarged, due to marked increase in size of the right ventricle, and may extend to the axilla.

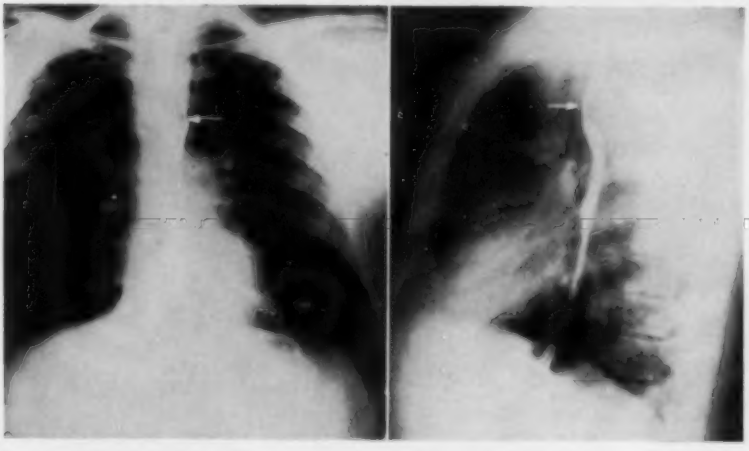

FIGURE 3: *Right Aortic Arch.* White male aged 32 years, asymptomatic. *PA View*: Esophagus deviated to the left at level of aortic arch. *Lateral View*: Esophagus deviated anteriorly at level of aortic arch.

X-ray films show a unique heart contour, consisting of a plateau silhouette caused by the single large vessel emerging from the enlarged ventricular mass. The truncus is so large that it conspicuously indents the esophagus along its left margin. In both oblique views it is also displaced backward sharply toward the spinal column. Abnormally large bronchial arteries arising from the large vessel through which the lungs receive their blood supply, due to the absence of the pulmonary arteries, may envelop the esophagus causing it to deviate from its normal course. Enlargement of the left auricle may result in a posterior displacement of the esophagus.

7. *Dextrocardia*

A reversal in the direction of the primitive cardiac loop results in dextrocardia. It is frequently associated with other cardiac abnormalities or a complete situs inversus. Uncomplicated dextrocardia produces no symptom.

X-ray films show an indentation of the esophagus on its right margin by the concomitant right aortic arch. The presence of a left aortic arch is abnormal, and, when present, it requires a search for other serious malformations of the heart.

Rheumatic Heart Disease

One or more cardiac chambers may be enlarged in rheumatic valvular disease depending upon the number and degree of valvular involvement. Left ventricular enlargement occurs to the left and posteriorly. Marked enlargements, especially those involving the inflow tract, may compress the lower end of the esophagus. The right ventricle enlarges to the left and anteriorly. Hence, an increase in this chamber alone rarely affects the esophagus. Left auricular enlargement is predominantly to the right and

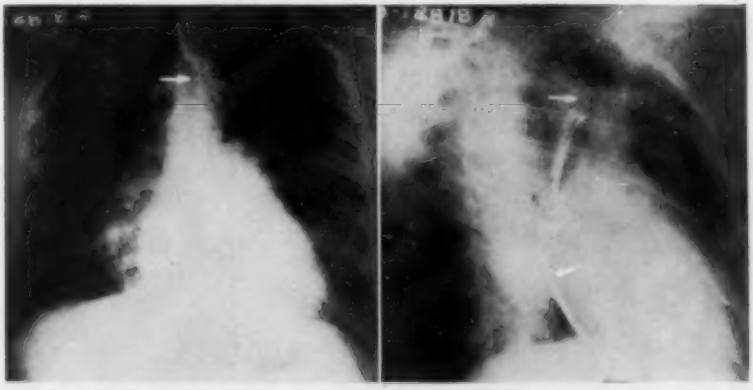

FIGURE 4: *Acquired Mitral Stenosis and Congenital Right Aortic Arch.* White male aged 38 years, no rheumatic history or symptomatology. Accidental finding of apical pre-systolic murmur with thrill and soft blowing systolic murmur, P2 greater than A2. EKG shows auricular changes only. *PA View*: Esophagus deviated to left at level of aortic arch. Prominent pulmonary artery complex. Absent aortic knob on left side. *RAO View*: Esophagus deviated anteriorly, characteristic of right aortic arch. Posterior esophageal displacement at the level of left auricle. Enlarged pulmonary conus.

posteriorly, and most frequently compresses the esophagus. It is well to remember that in the fibrillator without mitral disease, left auricular enlargement may also be quite striking. Right auricular enlargement is predominantly to the right and anteriorly, and less commonly affects the esophagus.

Recent papers (Sosman and others) have emphasized that the radiologist cannot exclude mitral disease by finding normal heart contours, or distinguish stenosis from insufficiency in many instances. Lateral views may prove helpful occasionally in such instances by revealing early chamber enlargement and compression of the esophagus (Fig. 7). On the other hand, both mitral stenosis and mitral insufficiency may cause a tremendous increase in size of the left auricle which, occasionally, may not displace the esophagus to the right and very little posteriorly.

1. *Mitral Stenosis*

The left auricle is the first chamber to enlarge in mitral stenosis, and may reach an enormous size owing to hypertrophy and dilatation. In most cases of long standing, x-ray findings are produced which are diagnostic. An enlarged left auricle is frequently found in combination with dilated pulmonary artery branches and prominent pulmonary conus. Since the left auricle lies posteriorly and rests on the esophagus, the slightest increase in size may compress the midportion of the esophagus backwards and to the right. This is readily recognized in the RAO view (See Fig. 4). Occasionally, the esophagus slides over the enlarged left auricle causing a displacement toward the left. The small aortic knuckle usually seen in mitral stenosis is caused partly by a true hypoplasia of the aorta, and partly by right ventricular rotation, resulting in displacement of the entire cardiac silhouette toward the left.

Swallowed barium passes normally to a point just below the left main bronchus, where it seems to halt momentarily. If the pulmonary artery is greatly distended, it pushes the left main bronchus backward and the

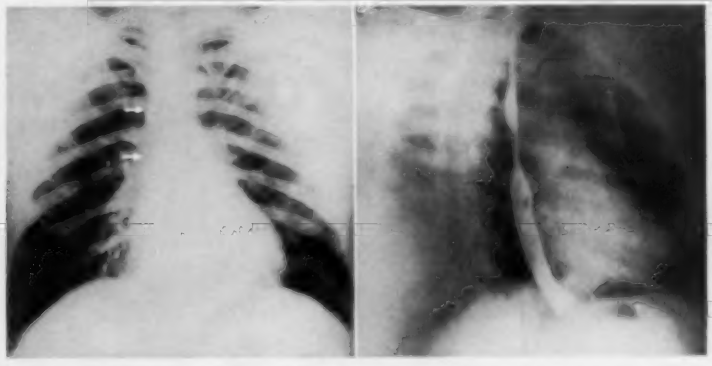

FIGURE 5: *Right Aortic Arch and Right Descending Aorta.* White male aged 29 years, without symptoms or physical findings. *PA View*: Esophagus slightly deviated to left at aortic arch level, indicating right aortic arch. *RAO View*: Esophagus is not displaced at level of aortic arch, indicating right descending aorta.

obstruction to barium passage appear higher up. The deviated bronchus may produce an extra impression on the esophagus. When marked enlargement of the left auricle exists, the passage of barium through the entire esophagus may take up to eight minutes. In the LAO view, there is no obvious esophageal displacement. On some occasions, minimal enlargement of this chamber may be visualized only in the right lateral view (See Fig. 7).

2. *Mitral Regurgitation*

Isolated mitral regurgitation results in an enlargement of the left auricle and may produce esophageal displacement.

3. *Tricuspid Lesions*

Tricuspid insufficiency and stenosis are rare. Their presence may be inferred from x-ray studies if there is considerable enlargement of the heart to the right, a relatively small left auricular impression on the esophagus, and absence of pulmonary congestion.

Luetic Aortitis

Diffuse inflammation of the aorta is by far the most common manifestation of syphilis of the cardiovascular system. Aortitis may eventually produce secondary effects on the heart. Esophageal compression almost never occurs without the existence of aneurysmal dilatation which may be saccular, fusiform or multiple. Aneurysms may not only compress the

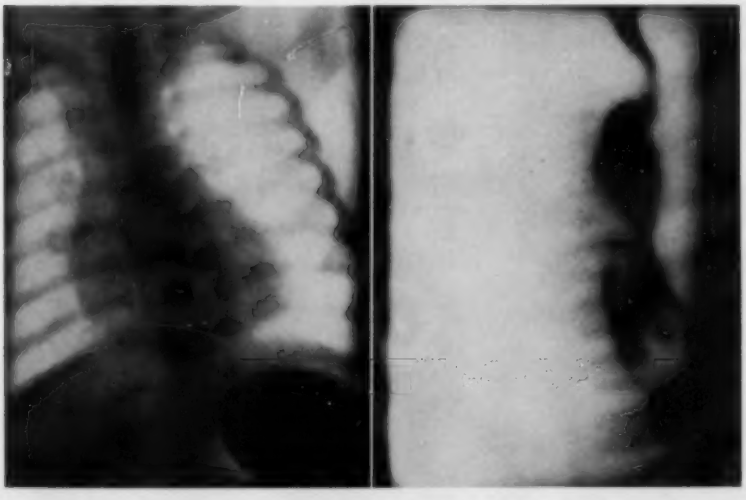

FIGURE 6: *Double Aortic Arch.* White male aged 3 months, with dyspnea on feeding. Transmitted pulsations seen on bronchoscopy at level of the arch. *PA View*: Lateral compression of esophagus bilaterally at level of aortic arch. *Lateral View*: Marked posterior indentation of esophagus with forward displacement at level of aortic arch and dilatation above this level (Courtesy Capt. C. F. Storey, USN, and Lt. J. W. Crittenden, USN, US Naval Hospital, St. Albans, L. I., N. Y.)

esophagus, producing dysphagia, but are also known to rupture into this structure on rare occasions.

X-ray films of aneurysm of the ascending aorta in the PA view may reveal a dense bulge of the right supracardiac shadow, with displacement and compression of the esophagus and trachea to the left (Fig. 8). Aneurysm of the transverse portion reveals a bulge to the left in the PA view, with displacement of the esophagus and trachea to the right (Fig. 9). In the LAO view, these structures may be pushed anteriorly. Aneurysm of the descending portion usually displaces the esophagus anteriorly, but it may be pushed to either side depending on the site of the aneurysmal bulge. Kymographic or tomographic studies further corroborate the presence of aneurysm. Incidentally, the wall of the ascending aorta should be carefully studied for evidences of calcification. Approximately half the cases of luetic aortitis reveal this finding as a healing stage.[6] Serologic tests are positive in approximately 85 per cent of cases, further excluding atherosclerosis as the causative factor.

Since luetic aortitis results in elongation, tortuosity and dilatation of the aorta, the esophagus is pulled to the left below the aortic knob by fibrous adhesions to the displaced aorta (See Fig. 8). In the LAO view, the esophagus is pulled posteriorly. Isolated aneurysms of the left carotid or subclavian arteries are rare, and seldom become large enough to produce esophageal compression. In such instances, a localized compression of the left esophageal margin may be observed above the position of the aortic arch.

Compression of the esophagus by luetic aneurysms may be mistaken for other disease processes. Hence, *differential diagnosis* must include bronchopulmonary malignancies, dermoid cysts, neurofibromata, lymphblastomata, bronchogenic cysts, Boeck's sarcoidosis, and other lesions. Pericardial

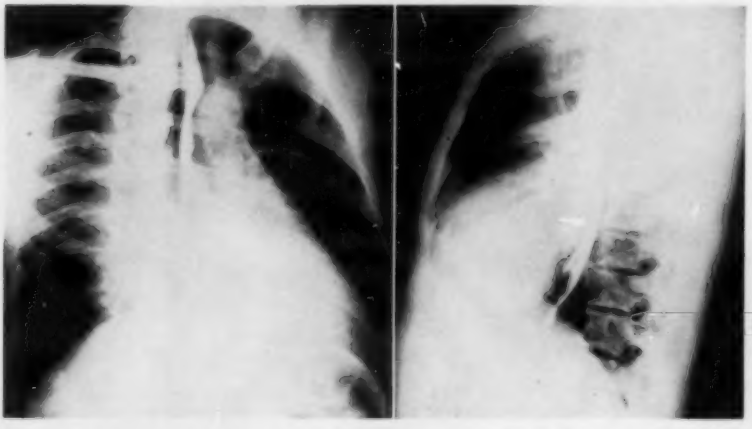

FIGURE 7: *Mitral Valvular Disease.* White male aged 24 years, with mitral stenosis and insufficiency. Normal EKG. *RAO View*: Esophagus does not show esophageal deviation. *Lateral View*: Esophagus deviated posteriorly by left auricular enlargement.

celomic cysts, esophageal dilatation due to cardiospasm, esophageal diverticulum, and diaphragmatic hernia may also cause confusion when evaluating such shadows, and it is important to determine their exact origin and position, as well as their relationship to the esophagus and to the heart, diaphragm and trachea. Most posterior mediastinal tumors prove to be of neurogenic origin, whereas those lying anteriorly are most frequently dermoids, teratomata, lipomata or lymphangiomata. Bronchogenic cysts are round, homogeneous and adjacent to the hilum. Pericardial celomic cysts or liver herniation produces a smooth round shadow which obliterates the cardiophrenic angle.

PA and lateral views are important. Fluoroscopy is of value in determining whether the mass remains connected to the diaghragm during deep inspiration. Thick barium ingestion may differentiate dysphagia of intrinsic origin from that caused by compression. When the aneurysm is unclotted, angiocardiography reveals filling, and kymography shows typical expansible pulsations. Fluorocardiography also permits the investigation and study of cardiac chambers and of the large vessels, as well as the motion of medium-sized hilar shadows not readily accessible by other means. Tomography may delineate cavitation within a mass. Such sectional x-ray films may also be helpful in localizing an undetermined mass. Bronchography, bronchoscopy with biopsy, and sputum staining are important in differentiating bronchopulmonary lesions. Diverticulum of the esophagus and hiatus herniation may be excluded by gastro-intestinal series. The latter condition is more discernible in the Trendelenburg position. Finally, a therapeutic test with irradiation for lymphblastomata, or with heavy metals and penicillin for luetic aneurysm, may be helpful on some occasions in arriving at the correct diagnosis.

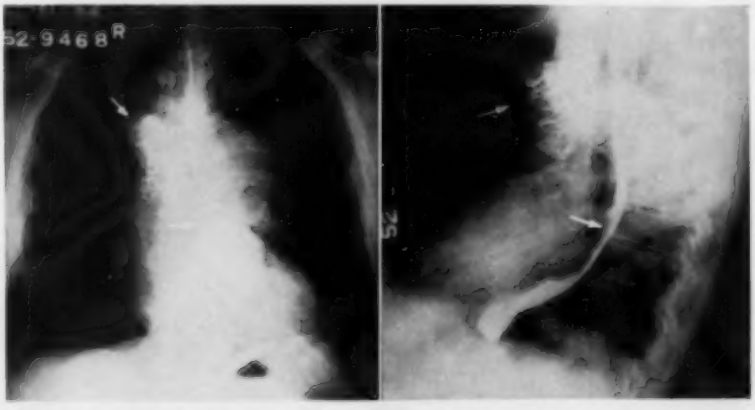

FIGURE 8: *Luetic Aortitis.* Colored male of 49 years, with shooting pains in chest and nocturnal dyspnea. Luetic history of 20 years. Supra-cardiac widening on percussion but no murmurs. Normal EKG. Kline test 4 plus. *PA View*: Note marked fusiform aneurysmal widening of ascending aorta which has been wired (upper arrow), and deviation of esophagus toward left (lower arrow) due to luetic aortitis of descending portion. *Lateral View*: Shows esophageal traction posteriorly due to luetic aortitis (lower arrow).

Atherosclerosis of the Aorta

Atherosclerosis is the most common of all disease processes affecting the aorta. This degenerative lesion causes the aorta to become sclerosed, elongated, tortuous and widened. The process may reach such extremes as to give rise to aneurysmal formation, although this appears more commonly in the abdominal aorta. This lesion usually produces no symptom, but abnormalities are commonly observed on x-ray films.

X-ray films may reveal tortuosity, elongation and prominence of the aortic knob. The knob may project into the left lung field, pulling the barium-filled esophagus to the left and posteriorly, and pushing the trachea to the right. In extreme cases, the esophagus may be found in the left paravertebral gutter or left chest. It is best visualized in the left anterior oblique position during deep inspiration. When the aortic deformity is severe, the descending portion may actually form a letter "S," as delineated by the barium-filled attached esophagus, or by marked sclerotic changes in the aorta itself. Although atherosclerotic aneurysms are rare in the thoracic aorta, those affecting the arch or descending portion may produce a localized compression of the esophagus.

In the PA view, there is displacement of the esophagus to the left and below the aortic indentation, caused by the pulling of normal fibrous attachments between the esophagus and the displaced aorta (Fig. 10). In the LAO view, the esophagus follows almost the identical course of the aorta owing to the common fibrous attachments. Although the esophagus is prevertebral in position normally, it becomes displaced to the left along the paravertebral gutter. In the RAO view, the esophagus is displaced posteriorly. Left auricular enlargement can be differentiated by the clear area of lung tissue between this chamber and the esophagus.

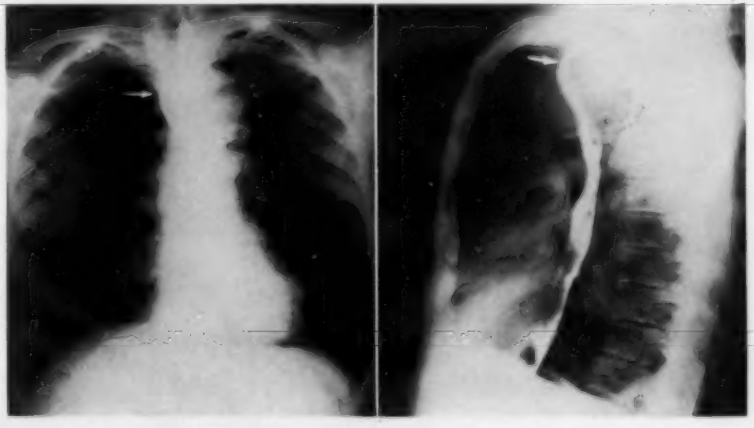

FIGURE 9: *Aneurysm of Arch of Aorta.* White male aged 60 years, with gastric complaints but no physical findings. BP 140/80. *PA View*: Esophagus deviated to right by saccular aneurysm of aortic arch. *Lateral View*: Esophagus deviated forward by saccular aneurysm of aortic arch.

Dissecting Aneurysm

Although the exact cause of this degenerative disorder remains unproved, most cases are attributed to cystic necrosis of the media.[1] The most frequent site of rupture occurs around 3 cm. above the aortic cusps. Severe chest pain radiating along the course of dissection, palpable abdominal masses are symptoms, and signs of involvement of any aortic branch may appear. Although most cases rupture into the pericardiac sac (tamponade) or left pleural cavity, rupture into the esophagus with hematemesis has also been described.

There are no characteristic signs revealed on x-ray films of dissecting aneurysm. However, serial roentgenograms may show a progressive aortic or supracardiac widening or deformity which increases in size either slowly or rapidly. In the oblique views, the esophagus may be displaced anteriorly as the dissection progresses. When rupture into the pericardium ensues, signs of cardiac tamponade become evident. Pericardial tap reveals the presence of blood. Kymograms and fluoroscopy shows small to absent pulsations despite an increase in the size of the cardiac shadow. Rupture into the mediastinum may compress the esophagus and result in dysphagia. Frequently, there is ecchymosis of the skin over the neck and chest. Direct rupture into the esophagus with severe hematemesis has also been described.

The following diseases have been simulated on various occasions and, hence, must be differentiated: coronary occlusion, embolism of large vessels, syphilitic aneurysm, solid mediastinal tumors and adhesive pleurisy. Coronary occlusion usually presents a history of angina pectoris, a more gradual development of pain of less severe nature and shorter duration, pericardial friction rub, and electrocardiographic changes. Embolism of a large vessel is, as a rule, associated with previous disease of the heart

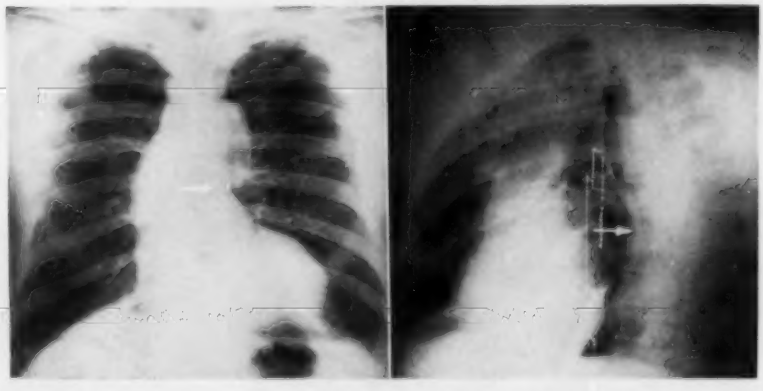

FIGURE 10: *Generalized Arteriosclerosis of Aorta.* White male aged 56 years, with no symptoms or physical findings. *PA View*: Widening and elongation of aorta, with marked displacement of esophagus to the left. *LAO View*: Widening and tortuosity of the aorta, pulling esophagus posteriorly due to fibrosis tissue connections.

or veins. Syphilitic aneurysm develops gradually and presents a history of earlier lesions, positive serologic tests, and a different clinical course.

Acknowledgment: We are indebted to Dr. William Dock for a review of this paper and suggestions.

CONCLUSIONS

1. Roentgenologic film and fluoroscopic diagnosis of many diseases of the heart and the aorta can be greatly aided by a careful examination of the barium-filled esophagus.

2. These cardiovascular lesions include congenital anomalies of the heart and aorta, rheumatic valvular disease (especially mitral stenosis), luetic aortitis, atherosclerosis of the aorta, and dissecting aneurysm.

CONCLUSION

1. El examen a los rayos X por fluoroscopía y la película puede ser adicionado en el diagnóstico de las enfermedades del corazón y de la aorta mediante un cuidadoso examen del esófago llenado con bario.

2. Estas lesiones cardiovasculares incluyen anomalías congénitas del corazón y de la aorta, enfermedad reumática valvularsis de la aorta y el aneurisma disecante.

RESUME

1. Le diagnostic radioscopique et radiographique de nombreuses affections du coeur et de l'aorte peut être grandement aidé par l'examen attentif de l'oesophage opacifié par la baryte.

2. Ces lésions cardiovasculaires comprennent des anomalies congénitales du coeur et de l'aorte, le rhumatisme valvulaire (particulièrement la sténose mitrale), l'aortite syphilitique, l'athérome aortique, et l'anévrysme dissèquant.

SCHLUSSFOLGERUNG

1. Die Diagnose vieler Erkrankungen des Herzens und der Aorta anhand von Röntgenaufnahmen und Durchleuchtungen kann erheblich erleichtert werden durch eine sorgfältige Untersuchung des mit Barium gefüllten Ösophagus.

2. Diese cardiovasculären Veränderungen umfassen angeborene Anomalien des Herzens und der Aorta, rheumatische Klappenerkrankung (besonders Mitralstenose), luetische Aortitis, Atherosklerose der Aorta und intramurales Aneurysma.

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The Use of Enzymes and Wetting Agents in the Treatment of Pulmonary Atelectasis

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Introduction

In April 1953, because of the serious problem of atelectasis in our poliomyelitic patients, a study on atelectasis was begun at the Rancho Los Amigos Respiratory Center for Poliomyelitis. One hundred twenty-five cases of atelectasis with only one failure are reported in this study.

The problem of atelectasis is not a new one and for many years has been a significant complication in postoperative abdominal general surgical cases. Even today, with improved anesthesia technics and the employment of a wide variety of antibiotics and chemotherapy, it is still a significant complication. More recently it has been noted that in post-poliomyelitic patients atelectasis is the most serious complication and the main cause of pulmonary disease which leads to death.

There have been various reports in the literature which give an incidence of postoperative atelectasis as high as 25 per cent in major upper abdominal surgery, and in our own experience at the Respiratory Center for Poliomyelitis the incidence in non-surgical post-poliomyelitic cases is approximately 30 per cent.

There are four factors which are prominent in the development of atelectasis. They are: (1) diminished respiratory function, (2) absent or ineffective cough, (3) abnormal bronchial secretions, both in quantity and in quality, and (4) respiratory infection. Although the etiology of the four factors is far different in poliomyelitic cases than in others, the common denominator in all atelectasis is the retention of viscid, tenacious secretions which cause obstruction of the airway to a whole lung, a lobe or a segment. Removal of these secretions, then, is the solution to the problem. This has not been easy to accomplish because of the extreme viscidity of the secretions in most instances, thereby rendering it impossible for the patient to expel the obstructing material. Once the secretions are thinned or liquefied, expulsion can be accomplished with facility.

It became obvious that some agent was necessary to thin out and loosen these tenacious secretions. We turned to the enzymes and wetting agents to find the solution.

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Of all the enzymes "tryptar" appeared to be the most promising and an article by Peck and Levin* gave us the stimulus to use it. Their results in two cases of long-standing atelectasis in post-poliomyelitic cases were striking. Among the wetting agents "alevaire," or a slightly modified formula called "triton A-20," was the best available. This was used in conjunction with the "Mist-O_2-Gen" apparatus of Dr. Clarence Denton.

"Tryptar" is a highly purified crystallin trypsin derived from mammalian pancreas gland. It is effective over a pH range of five to eight but exhibits its greatest activity at pH 7.1. It has a broad spectrum of proteolytic action on proteins, mucins, fibrin and protein-split products. It is not active on and does not harm living tissues and cells. The effect which we were concerned with in this study was the action on bronchial secretions and in this instance it liquefied or thinned out the secretions by dissolving the mucin so prominent in bronchial secretions. "Triton A-20," the wetting agent, lowers the surface tension of the droplets and causes them to be deposited on the mucosa in vastly greater numbers. In addition, this detergent exerts a liquefying effect on mucopurulent secretions. The liquefying effect is obtained by lowering the surface of the respiratory secretions.

Once the secretions are liquefied the next important step is the removal of them. In atelectasis these secretions are found not only in the major bronchi but in the majority of instances obstructing the smaller bronchi, bronchioles and alveoli. Removal of the secretions from these areas in the lung is an important factor. In non-poliomyelitic patients this is accomplished by inducing the patient to cough by whatever means is found necessary. Only by an adequate cough can these secretions be removed, no matter whether a tracheotomy is present or not. A catheter can reach only secretions in the trachea, mainstem bronchi or even down to the tertiary bronchi, but no further. In the post-poliomyelitic patient coughing becomes an extremely complex problem. Most severe poliomyelitic patients have no cough or one which is completely ineffective. Thus, they must be coughed artificially.

Materials and Methods

The patients reported in detail are those at the Respiratory Center for Poliomyelitis. Only brief comments will be made on non-poliomyelitic patients treated at three private hospitals and one County Hospital in the County of Orange, California.

All patients in this study had definite atelectasis by x-ray film and all reported as clear showed complete clearing by x-ray. The only enzyme used was aerosol "tryptar" and the only aerosol wetting agent used was "triton A-20," a 25 per cent solution of "alevaire" which is an aqueous solution of a new detergent, "triton WR-1339," 0.125 per cent, in combination with sodium bicarbonate two per cent and glycerin five per cent.

There were three methods used in administering "tryptar": (1) by direct instillation through a bronchoscope into the bronchus of the lobe

*Peck, M. E. and Levin, S.: *J. Thoracic Surg.*. 24:619, 1952.

or lung involved, (2) by aerosolization through a tracheotomy tube, and (3) by aerosolization with a conventional mask used for aerosol treatments. With method one, 125 to 250 mg. of aerosol "tryptar," dissolved in five cc. of Sorensen's Buffer Solution is placed directly into the bronchus of the affected lobe or lung. This is used both in tracheotomized and non-tracheotomized patients. The patient is kept in the position which makes the involved portion of lung dependent for one hour. Then, he is moved back to the normal position and induced to cough. This method was used as often as necessary to clear the lung and serial x-ray films daily determined this. Usually two or three treatments at intervals of two to three days were sufficient to clear the atelectasis. Method two consists of the following: 125 mg. of aerosol "tryptar" dissolved in approximately three cc. of Sorensen's Buffer Solution is placed in the nebulizer (DeVilbiss No. 40). To this is added five to seven drops of 1:200 isuprel hydrochloride for bronchial dilation. The appropriate antibiotic is then dissolved in this solution so there is no more than four to four and one half cc. total solution. (Aureomycin and terramycin are incompatible with "tryptar.") The oxygen is set to deliver five liters per minute and the treatment is continued until all solution has been nebulized. It takes approximately 30 minutes for the full treatment. This treatment is interrupted if the patient must cough, or if tracheal aspiration is necessary. Method three uses exactly the same solution and oxygen setting as for method two. The only difference in the two methods is the route of delivery, method three using the mask for delivery through the nose and mouth. This treatment likewise may be interrupted as necessary for coughing. Both methods two and three are given three or four times a day, as is deemed necessary. In all three methods 30 to 45 minutes prior to giving the treatment, 50 mg. of benadryl, either orally or by hypodermic, is given to counteract any minor side effects which may occur.

Methods of administering "triton A-20" were three: (1) by tent with a nebulized solution flowing into the tent which covered primarily the head and neck of the patient, (2) by mask, and (3) by tracheotomy tube. Method one consists of nebulization of the "triton A-20" solution by the use of the "Mist-O_2-Gen" apparatus. This apparatus is placed directly inside the tent so that a good concentration of mist is present at all times. The head and neck of adults were covered by the tent and in children the whole body was usually enclosed. This method was not used on respirator patients. Method two consists of delivery of the nebulized "triton A-20" by mask to the patient. Nebulization was also accomplished by the use of the "Mist-O_2-Gen" apparatus. Method three was the same as method two except that delivery was through the tracheotomy tube by means of a special attachment also supplied by Dr. Clarence Denton. For all three of these methods the length of time for treatment was the same. Each new patient treated with the wetting agent was put on "triton A-20" therapy for 10 to 12 hours. Then on one hour and off one hour during the next 24 hours; then on two hours and off two hours for the duration of treatment. Method two created some difficulty because

of the discomfort to the patient in wearing a mask for such long periods of time.

Coughing is accomplished in various ways depending on the type of patient. In non-poliomyelitic patients who cannot or will not cough voluntarily, tracheal catheterization is the best means of producing a cough in both tracheotomized and non-tracheotomized patients. In post-poliomyelitic patients the coughing which is extremely important must be done by artificial means. For patients with tracheotomies and in a respirator the vacuum cleaner machine is attached to a porthole in the respirator and the pressure decreased to a negative 40 cm. of H_2O; this produces a deep inspiration. When this pressure is reached the bedpan port is suddenly

FIGURE 1: Atelectasis, right upper and lower lobes. Treated by aerosol "tryptar" for two weeks with vacuum machine coughing. Complete clearing is shown in three weeks.

FIGURE 2: Complete atelectasis, right upper lobe. Treated with aerosol "tryptar" and vacuum coughing, 10 days. Complete clearing in two weeks.

FIGURE 3: Complete atelectasis right upper lobe, partial atelectasis left upper lobe. Aerosol "tryptar" and vacuum machine coughing used for two weeks. Middle x-ray film shows almost complete clearing of right upper lobe but progression of left lung atelectasis one week following start of treatment. Third x-ray film reveals complete clearing of both lungs four weeks following start of treatment. This patient had atelectasis for five months prior to starting treatment which was not cleared by any former treatment including bronchoscopy three times.

opened and a satisfactory expulsive force is produced through the open tracheotomy tube. A series of 24 coughs are given four times a day. The trachea is aspirated as necessary to clear the air passages of secretions. In post-poliomyelitic patients without tracheotomy tubes the vacuum cleaner method cannot be used because synchronization of the action of opening the glottis with the sudden expulsive force is difficult or impossible in almost all patients. Therefore "manual coughing" is used. With this method the attendant compresses the thorax synchronous with the expiratory phase of the respirator. Although "manual coughing" is not as effective as vacuum coughing, it serves the purpose in the cases where it is used. These coughing procedures are used according to patient type regardless of whether "tryptar" or "triton A-20" is used.

Antibiotics are administered in all cases both by aerosol and parenterally as indicated. Aerosol antibiotics are not used in patients receiving "triton A-20" therapy because of the large amounts of solution necessary. All patients receive parenteral antibiotics during the course of treatment. Antibiotics are used according to sputum culture and sensitivity tests if feasible.

Results

In 30 cases of atelectasis occurring in non-poliomyelitic cases treated at three private hospitals and one county hospital in the County of Orange, California, not one failed to clear in three to four days. In most instances complete clearing was noted in 48 hours. All of these non-poliomyelitic patients were treated with "tryptar," the "triton A-20" and "Mist-O_2-Gen" apparatus not being available. Nine patients had tracheotomies and complete clearing was noted in all of these within 48 hours. There was no death in this group. Bronchoscopy was not necessary in any patient in this group.

Results of treatment of 95 cases of atelectasis occurring in post-poliomyelitic patients are presented in more detail. Atelectasis in these patients is much more insidious and complex and more difficult to clear. The absence of a voluntary cough with markedly diminished respiratory function and the altered pulmonary physiology in general, incident to poliomyelitis make the complication of atelectasis an extremely serious problem in these patients.

The 95 cases reported here were arbitrarily broken down into two groups, "chronic" and "acute." Chronic atelectasis was set at duration of two weeks and over, and acute atelectasis under two weeks. There were 47 chronic and 48 acute cases (Table I). Involvement by lobes is shown and it is interesting to note that 35 cases had involvement of the right upper lobe. The primary cause of this is poor drainage of this lobe in the supine position.

Table II shows the types of treatment, the number of acute or chronic patients treated in each category, and the final results of treatment. There were nine patients treated with "triton A-20" who failed to clear or had a spread of the atelectasis. These nine patients were then treated with "tryptar" and are included under that heading also. Of the 88

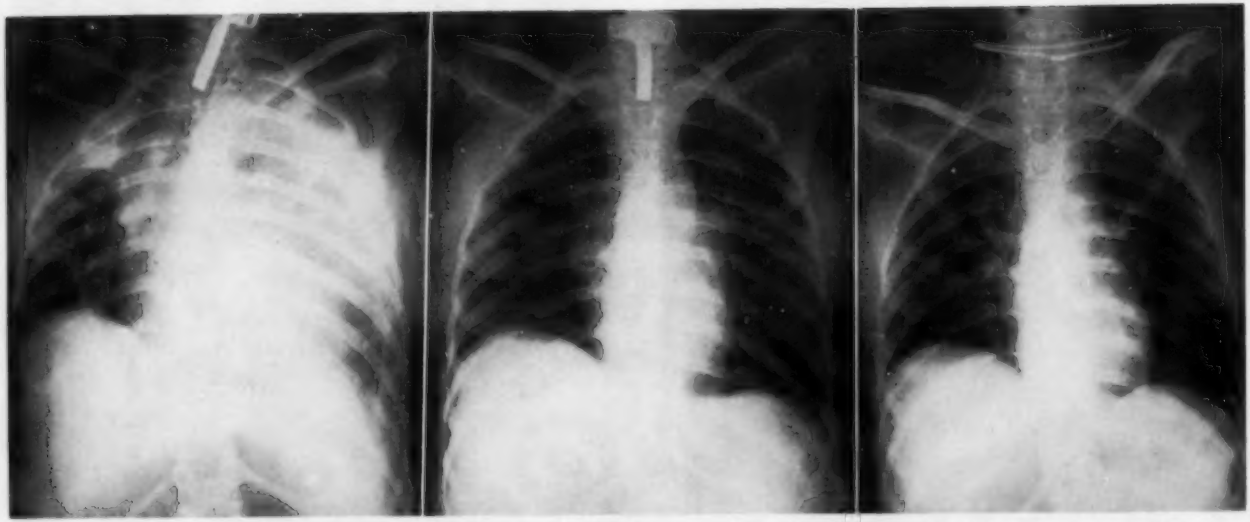

FIGURE 4: Complete atelectasis left lung; complete atelectasis right upper lobe. The patient had had atelectasis for three months prior to instituting aerosol "tryptar" and vacuum coughing. Patient also had been bronchoscoped two times in addition to all other forms of treating atelectasis before being put on aerosol "tryptar" and vacuum coughing. The middle x-ray film shows almost complete clearing after patient had been on aerosol "tryptar" for two weeks. The third x-ray film shows complete clearing six weeks following start of aerosol treatment.

patients treated with "tryptar" there was only one failure. This was in a female who had a completely paralyzed diaphragm which compressed the involved lung markedly. She had had atelectasis for five months when treatment was started. There were actually 16 patients treated with "triton A-20" but as stated above there were nine failures who were then treated with "tryptar" and cleared completely under this treatment. It can readily be seen that "tryptar" is the most successful agent. "Triton A-20" was less than 50 per cent effective in clearing atelectasis, whereas "tryptar" was more than 95 per cent successful. When comparing "triton A-20" and "tryptar" as to length of time necessary for complete clearing, "tryptar" was successful in clearing 68 per cent of the acute cases and 42 per cent of the chronic cases in two weeks. "Triton A-20" cleared only 14 per cent of the acute cases and none of the chronic cases in two weeks.

TABLE I
CLASSIFICATION AND DISTRIBUTION OF ATELECTASIS

Classification*		No. of Patients
Acute	2 weeks or less	48
Chronic	2 weeks to 3 months	31
	3 months to 6 months	12
	Over 6 months	4
	TOTAL	95

DISTRIBUTION

Right Lung		Left Lung		Bilateral
RUL	35	LUL	2	10
RML	3	LLL	14	
RLL	6	All Lobes	5	
RUL, RML	2			
RML, RLL	10			
All Lobes	8			
Total	64		21	10

*Based on time since onset of atelectasis before this treatment started.

TABLE II
RESULTS

Type of Treatment	No. Pts. Treated	No. Pts. Cleared			Failures
		Acute	Chronic	Total	
Triton A-20 with Mist-O_2-Gen apparatus	16	5	2	7	9*
Tryptar by bronchoscopic instillation	11	1	9	10	1
Tryptar by aerosolization	77	42	35	77	
Total	88	43	44	87	1

*These nine failures were switched to tryptar and all cleared.

In general the length of time required to clear atelectasis in post-poliomyelitic cases was directly proportional to its duration. The longer it was present the longer it required to clear. Out of the 95 cases there were 16 in whom atelectasis had been present for over three months. All of these cleared except for the one failure which was in this group. There were two deaths in this series. One was due to severe genito-urinary sepsis with bilateral staghorn calculi; the atelectasis had been cleared for four months with no evidence of recurrence. The other death was in the one failure of the series. This patient had multiple abscesses in the right lung with metastatic brain abscesses. Figures one through five represent examples of post-poliomyelitic patients treated in this series.

Toxicity

Toxicity or side reactions to the use of "tryptar" are so minor that they are not significant. There is much being said about serious reactions and even anaphylactic reactions attributed to the use of "tryptar." This study represents the use of aerosol "tryptar" in well over 10,000 individual treatments. The only reactions noted were mild flushing of the face and a sensation of heat in the face in only four patients. With the use of benadryl as described above there have been no further reactions. We have yet to see an anaphylactic reaction to "tryptar." We believe that the so-called "reactions" described are due to flooding of the tracheo-bronchial tree by the secretions which are liquefied by the "tryptar." Careful attention to removal of these liquefied secretions will avoid these so-called "reactions." There has been no reaction of any type with the use of "triton A-20."

Discussion

We do not wish to intimate that all that is necessary to clear atelectasis is the administration of "tryptar" or "triton A-20" by aerosol. It must be

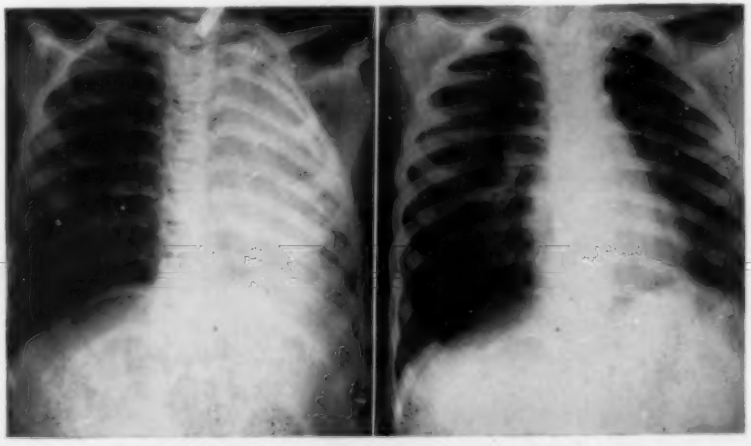

FIGURE 5: Complete atelectasis left lung. Aerosol "tryptar" and vacuum coughing used on this patient for one week. Complete clearing shown in 10 days.

emphasized, *first*, that once the secretions are liquefied, a cough is necessary to expel or to move them up to point where they can be reached with the aspirating catheter. In non-poliomyelitic patients who cannot or will not cough voluntarily, tracheal catheterization will induce an adequate

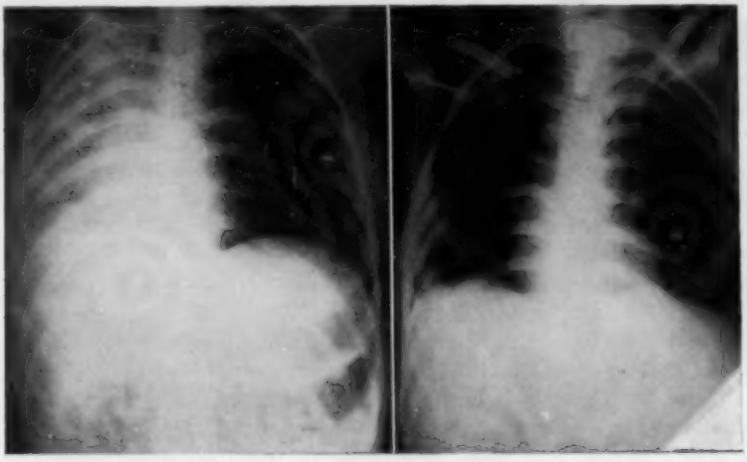

FIGURE 6: Complete atelectasis of the right lung. The patient was treated by bronchoscopy with instillation of "tryptar" into the right main stem bronchus without clearing. Tracheotomy was recommended but the patient refused to have tracheotomy done for four weeks. No clearing was noted at the end of this four weeks and the patient finally consented to have tracheotomy done. With tracheotomy, aerosol "tryptar," and vacuum coughing the patient completely cleared the atelectasis within two weeks.

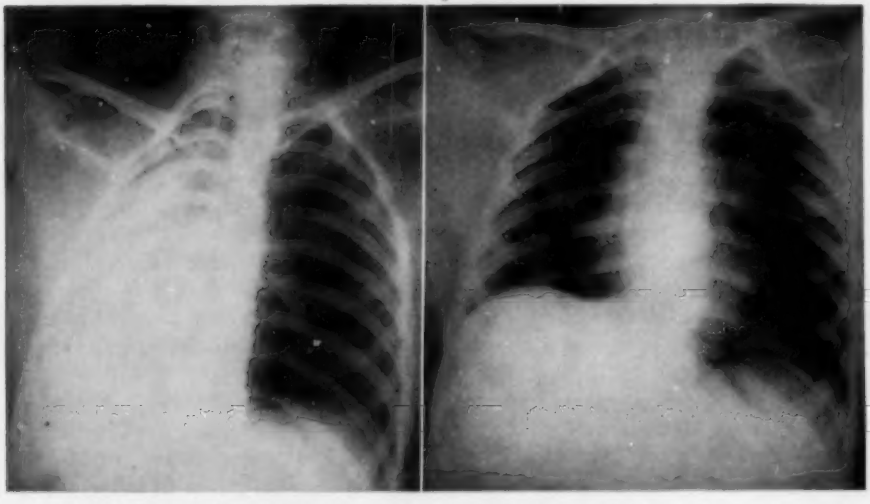

FIGURE 7: Complete atelectasis, right lung. Patient refused tracheotomy. She was treated for two weeks on aerosol "tryptar" and vacuum coughing without clearing. After tracheotomy was done she cleared the right lung completely within five days on continued aerosol "tryptar" and vacuum coughing.

cough, both in the tracheotomized and non-tracheotomized patient. In poliomyelitic patients who cannot or who have a weak cough, this is best accomplished at our institution by the use of the vacuum cleaner machine.

Second.—Another extremely important part of the total treatment of atelectasis, particularly in the poliomyelitic patient, is the tracheotomy. In patients with atelectasis who have no cough, or who are not cooperative, or who are unconscious, tracheotomy is most essential. In several instances in our series atelectasis failed to clear until tracheotomy was done (figures six and seven) ; then clearing of the atelectatic areas was prompt.

Third.—Upper respiratory infections play an extremely important part in providing an increase in secretions which may eventually lead to atelectasis. In the poliomyelitic cases we have found that an upper respiratory infection must be treated vigorously as a prophylactic measure in preventing atelectasis.

Fourth.—Antibiotics are, of course, also very important and were used both by aerosol and parenterally in all cases. The type of organism present in the atelectatic lung is significant. We have found our most resistant cases in patients who have as a predominating organism Pseudomonas aeruginosa, or Proteus vulgaris, which are insensitive to most of the antibiotics. The antibiotics which were used were given as indicated by sensitivity tests on the organisms found in the tracheobronchial tree.

SUMMARY

1. Atelectasis is a common serious complication in both poliomyelitic patients and non-poliomyelitic patients, but is a much more complex problem in the former.

2. In patients who have atelectasis the secretions are thick, viscid and tenacious and in most instances purulent. They must be loosened and thinned to make removal more easy. This is best accomplished by the use of aerosol "tryptar" which is safe and easily administered by mask or through a tracheotomy tube.

3. A cough is absolutely essential in the treatment of atelectasis because an adequate means of moving the secretions once loosened is extremely important. Without adequate coughing, failures in treating atelectasis are inevitable. In non-poliomyelitic cases this coughing is best induced by tracheal catheterization. In poliomyelitic patients who have no cough this is done best by artificial means.

4. Aspiration of secretions during aerosol treatment and with coughing is essential in order to prevent flooding of the tracheobronchial tree by the liquefied secretions.

5. Tracheotomy is essential in most instances in patients who have little or no cough of their own or in those who are unconscious, because it is impossible to aspirate secretions adequately without a tracheotomy opening.

6. The so-called "reactions" to "tryptar" are actually due to inadequate removal of the secretions which have been liquefied by "tryptar" and thus flooding the tracheobronchial tree.

7. Atelectasis in non-poliomyelitic patients responds successfully to

the use of "tryptar" within one to four days. Bronchoscopic aspiration is not necessary. In 30 cases treated with "tryptar" there was no failure.

8. In 88 cases of atelectasis in post-poliomyelitic cases "tryptar" was successful in clearing completely 87. In an additional 16 treated with "triton A-20," seven cleared completely and the other nine were switched to "tryptar" with clearing.

9. In the post-poliomyelitic group of cases there were two deaths, one completely unrelated to atelectasis, the other because of a severe atelectasis with abscess formation in the involved lung.

RESUMEN

1. La atelectasia es una complicación común tanto en los enfermos poliomielíticos como en otros, pero en los primeros el problema es más complejo.

2. En los enfermos que tienen atelectasia las secreciones son espesas, viscosas, tenaces y en la mayoría de los casos son purulentas. Deben ser licuadas y ablandadas para poder extraerlas con facilidad. Esto es obtenido mejor con aerosol de Tryptar que es seguro, facilmente administrado por mascarilla o a través de un tubo de traqueotomía.

3. La tos es absolutamente esencial en el tratamiento de la atelectasia, porque un modo apropiado de desplazar las secreciones es extremadamente importante. Sin tos eficaz los fracasos del tratamiento de la atelectasia son inevitables. En los casos sin polio esta tos se provoca mejor por la cateterización traqueal. En los poliomielíticos que no tosen esto es obtenido por recursos artificiales.

4. La aspiración de las secreciones durante el aerosol y la tos son esenciales para evitar la inundación debida a las secreciones licuadas.

5. La traqueotomía es esencial en la mayoría de los enfermos que no tosen o tosen poco o en los que están inconscientes porque es imposible aspirar las secreciones satisfactoriamente sin la abertura de la traqueotomía.

6. Las llamadas reacciones al Triptar de hecho se deben a una inadecuada extracciœn de las secreciones que se han licuado por esemedio y que inundan el árbol traqueobronquial.

7. La atelectasia en la poliomielitis responde bien al uso del Tryptar dentro de uno a cuatro días. La aspiración broncoscópica no es necesaria. En 30 casos tratados con Tryptar no hubo fracasos.

8. En 88 casos de atelectasia en post-poliomielíticos el Tryptar tuvo éxito para aclarar la atelectasia en 87.

Además, 16 tratados con Triton A-20 se limpiaron completamente y los otros nueve se cambiaron a Tryptar con buen resultado.

9. En el grupo post-poliomielítico hubo dos muertes, una completamente sin relación con la atelectasia y la otra a causa de una atelectasia severa con formación de absceso en el pulmón afectado.

RESUME

1. L'atélectasie est une complication habituelle et grave aussi bien chez les malades atteints de poliomyélite que chez les autres. Mais elle est un

problème infiniment plus complexe lorsqu'il s'agit des malades du premier groupe.

2. Chez les malades atteints d'atélectasie, les sécrétions sont épaisses visqueuses, tenaces, et dans la plupart des cas purulentes. Elles doivent être diluées et fluidifiées pour en rendre le rejet plus facile. Ceci est produit au mieux par l'utilisation d'aérosols de "tryptar" qui est sans danger et administré facilement par masque, ou à l'aide d'une canule laryngée.

3. La toux est un facteur absolument essentiel dans le traitement de l'atélectasie parce que c'est un moyen qui permet de rejeter les sécrétions une fois qu'elles sont fluidifiées. Sans toux, les échecs du traitement de l'atélectasie sont inévitables. Dans les cas de malaises non poliomyélitiques, cette toux est provoquée le plus facilement par cathétérisme trachéal. Chez les malades atteints de poliomyélite, qui n'ont aucune toux, elle doit être provoquée par des moyens artificiels.

4. L'aspiration des sécrétions pendant le traitement par aérosol et par la toux est essentiel pour ampêcher l'invasion de l'arbre bronchique par les sécrétions fluidifiées.

5. La trachéotomie est indispensable dans la plupart des cas chez les malades qui ont peu ou pas de toux, ou chez ceux qui sont inconscients, parce qu'il est impossible d'aspirer les sécrétions sans ouverture trachéale.

6. Les soi-disant réactions au "tryptar" sont dues au rejet incomplet des sécrétions qui ont été liquéfiées par le "tryptar" et qui envahissent l'arbre bronchique.

7. L'atélectasie chez les malades non poliomyélitiques peut être traitée de façon satisfaisante par l'utilisation de "tryptar" pendant un à quatre jours. L'aspiration bronchoscopique n'est pas nécessaire. Dans trente cas traités par le tryptar, il n'y eut aucun échec.

8. Dans 88 cas d'atélectasie, chez des malades ayant eu une poliomyélite, l'action du tryptar fut satisfaisante, en opérant un nettoyage complet chez 87 d'entre eux. En outre, chez 16 malades traités par le "triton A.20" sept eurent un nettoyage complet et les neuf autres furent remis au "tryptar" avec nettoyage.

9. Dans le groupe de malades ayant été atteints de poliomyélite, il y eut deux décès, l'un sans aucune relation avec l'atélectasie, l'autre à cause d'une atélectasie grave, avec formation d'abcès dans le poumon atteint.

ZUSAMMENFASSUNG

1. Die Ate'ektase ist sowohl bei Poliomyelitis-Patienten als auch bei anderen Kranken eine häufige und ernste Komplikation.

2. Bei Patienten mit Atelektase ist das Sekret dick, zähflüssig und meistens eitrig. Das Sekret muss gelöst und verdünnt werden, um seine Ausstossung leichter zu gestalten. Am besten wird dieses durch die Benutzung des Aerosols "Tryptar" erreicht, das leicht und zuverlässig durch eine Maske oder durch eine Trachealkanüle zugeführt werden kann.

3. Bei Behandlung der Atelektase ist der Husten unbedingt erforderlich, weil das gelöste Sekret hinausbefördert werden muss. Ohne adäquaten Husten sind Fehlschläge bei der Behandlung der Atelektase unvermeidlich. Bei Nicht-Poliomyelitis-Kranken wird dieses Husten am

einfachsten durch Katheterisierung der Trachea herbeigeführt. Bei Poliomyelitis-Patienten, die keinen Husten haben, wird dieser am besten auf künstliche Weise erzeugt.

4. Absaugung des Sekretes während einer Aerosol-Behandlung und beim Husten ist notwendig, um eine Überschwemmung des Tracheo-Bronchialbaumes durch das verflüssigte Sekret zu vermeiden.

5. Tracheotomie ist meistens bei den Patienten notwendig, bei denen wenig oder kein Husten vorhanden ist oder die bewusstlos sind, weil es unmöglich ist, das Sekret ohne Tracheotomie-Öffnung hinreichend abzusaugen.

6. Die sogenannten "Reaktionen" auf "Tryptar" sind in Wirklichkeit auf ein unzureichendes Entfernen des Sekretes zurückzuführen, indem durch "Tryptar" verflüssigtes Sekret den Tracheo-Bronchialbaum überschwemmt hat.

7. Bei Nicht-Poliomyelitis-Patienten führt die Anwendung von "Tryptar" innerhalb 1 - 4 Tagen zur Beseitigung der Atelektase. Bronchoskopische Absaugung ist nicht notwendig. Bei 30 mit "Tryptar" behandelten Patienten gab es keinen Misserfolg.

8. Bei Poliomyelitis-Patienten wurde in 87 von 88 Fällen die Atelektase durch "Tryptar" beseitigt. Bei 7 Patienten von 16, die mit "Triton A-20" behandelt wurden, kam es zu einem Verschwinden der Atelektase; die anderen 9 wurden der "Tryptar"-Behandlung zugeführt, wodurch auch bei diesen die Atelektase beseitigt wurde.

9. In der Poliomyelitis-Gruppe kam es zu 2 Todesfällen, von denen der eine keinerlei Beziehung zur Atelektase hatte, während der andere durch schwere Atelektase mit Abszessbildung in der befallenen Lunge ad exitum kam.

We wish to express our appreciation to the Armour Laboratories of Kankakee, Illinois for furnishing the "tryptar" for the original portion of this study.

Lipoid Granuloma of the Lung of Exogenous Origin

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A considerable variety of pathological states are associated with the abnormal appearance of lipids within the lung (Table I). Lipids arising within the body may be the cause of pulmonary lesions but these substances are themselves the result of some pathological process already present and are not the subject of this discussion.

Injury to the lung produced by lipids of exogenous origin is chiefly a disorder of the modern era and might even be considered, in part, as a complication of medical progress, since materials employed by the physician (mineral oil, oily nose drops, vitamin oils, iodized oil contrast media) are commonly the offending agents. In spite of this association, the injurious effect of oily substances on the lung was not promptly recognized. Mineral oil has been used for medicinal purposes since 1869[1] but it was not until 1920 that Guieysse-Pellissier[2] directed attention to the importance of oil aspiration after observing its effect on animals. Five years later (1925), Laughlin[3] published the first case reports of lipoid pneumonia in man; and Pinkerton[4] in 1928 worked out the variations in the pathological response which may occur when pulmonary tissues are exposed to oils of various derivations. During the ensuing decade, an increasing number of cases of oil aspiration pneumonia were reported, and Kaplan[5] in 1941 was able to collect 411 examples of the disease, 68 per cent of which were due to mineral oil, 23.4 per cent due to cod liver

TABLE I
CLASSIFICATION OF PULMONARY DISORDERS ASSOCIATED WITH LIPIDS OF ENDOGENOUS ORIGIN

1.	Cholesterol pneumonia—secondary to any suppurative disease of the lung:
	a. Bronchogenic carcinoma with bronchial obstruction and associated pneumonitis.
	b. Lobar pneumonia.
	c. Bronchopneumonia.
	d. Bronchiectasis.
2.	Lipoid reticulo-endotheliosis:
	a. Gaucher's disease.
	b. Niemann-Pick's disease.
	c. Hand-Schuller-Christian disease.
	d. Eosinophilic granuloma.
3.	Fat embolism.
4.	Ruptured dermoid cyst.[13]

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oil, 4.8 per cent due to butter fat, and 1.8 per cent due to iodized poppy seed oil. In 1943, Sweeney[6] reviewed 264 cases of lipoid pneumonia. These patients were almost equally divided between adults (131) and infants and children (133). Mineral oil used intranasally or as a laxative was the causative agent in 126 instances and was implicated in an additional 22 cases. Vitamin oils were a chief or contributing cause of pneumonitis in 67 patients, the vast majority of whom were infants and children. Since these studies were carried out, a number of other oily materials have been added to the list of agents which have been recognized as the cause of pulmonary lesions (Table II), but lipoid pneumonitis due to the majority of these substances is rarely encountered. Considerable emphasis has been placed on the hazards of mineral oil aspiration, and the use of oily nose drops has decreased in popularity, leading to a probable decrease in the incidence of the disease. Nevertheless, liquid petrolatum used orally or intranasally continues to occupy the position of chief offender and pulmonary changes due to its presence are still encountered with some frequency.

TABLE II
CLASSIFICATION OF PULMONARY DISORDERS PRODUCED BY LIPIDS OF EXOGENOUS ORIGIN

1. Lipoid pneumonia or granuloma—due to aspiration of oily substances:	
	Mineral oil, oily nose drops, cod liver oil, halibut liver oil,[5] viosterol,[5] castor oil,[5] olive oil,[5] cottonseed oil,[5] vaseline,[11] gasoline,[1] kerosene,[1] diesel,[1] nebulized industrial oil.[1]
2. Lipoid granuloma—due to deliberate intratracheal instillation of diagnostic materials:	
	Iodized poppyseed oil (Lipiodol,[5, 10])
	Iodized peanut oil (Iodochloral[9])
3. Regurgitation lipoid pneumonia—due to aspiration of lipid-containing foods (milk, egg-yolk):	
	Premature infants.
	Senile or debilitated individuals.
	Bulbar palsy.
	Laryngeal paralysis.
	Tracheo-esophageal fistula.
	Cardiospasm.

In spite of the attention which has been directed toward this subject, the medical profession in general has been slow to develop an awareness of the disorder. In many, if not most, of the reported cases in adults, the presence of a lipoid granuloma was not considered or even suspected prior to surgery, and we have been similarly surprised when the correct diagnosis was established by the pathologist. Much of what follows has been said before, but it would appear that any amount of reiteration is justified as long as the same mistakes continue to occur.

When lipid substances gain entrance to the lung the tissue response

which is invoked may vary from (1) an acute pneumonitis to (2) a chronic diffuse pneumonitis to (3) a chronic localized granuloma, depending on the type of oil, the quantity, the frequency with which it enters the lung, and perhaps the age of the patient.[7, 8] It is with the latter type of chronic localized reaction that this paper particularly concerns itself since these lesions are the most difficult to recognize and may defy every diagnostic procedure short of exploratory thoracotomy and histological study of biopsy material.

Localized lipoid granulomas apparently occur as the result of repeated aspiration of small quantities of a relatively inert material which has a large molecular size and thus cannot be readily transported from the lung or metabolized.[9] These lesions are therefore relatively permanent and may be first detected in the course of a routine roentgenographic examination many years after the source of oil has been removed and its history almost forgotten. Such a lesion assumes particular importance in that it frequently cannot be distinguished from a pulmonary neoplasm. In fact, the manner in which lipoid granuloma may mimic bronchogenic carcinoma is truly amazing, and in our opinion the diagnosis is not only difficult but at times may be impossible without resort to surgical exploration and direct biopsy of the lesion.

Efforts to define a reliable clinical picture of lipoid granuloma of the lung have been made in the past with little success. Symptoms may be entirely absent or may include cough, thoracic pain, dyspnea and hemoptysis, which are so common to a great variety of pulmonary disorders. Physical findings are in no way helpful in establishing an etiological diagnosis. It has been stated that the roentgenographic finding of "a rather homogenous shadow with sharply defined peripheral limits and a contrasting featuring of density at its hilar aspect . . . is a particularly valuable diagnostic sign,"[7] but this has not been helpful in our experience. The lesions are often bilateral and tend to occur in the posterior divisions of the lower lobes—somewhat more frequently on the right—but in many instances the lesions are solitary, circumscribed, and involve only the middle or upper lobes.

Admittedly, then, the diagnosis of lipoid granuloma of the lung is not easy; however, when lesions are multiple and bilateral, the diagnosis can be made with reasonable assurance in many cases, if the physician is (1) aware of the condition; (2) considers it in his differential diagnosis; (3) takes a careful history with reference to the possible aspiration of oily materials; and (4) studies sputum specimens for oil content. Undoubtedly, the key to correct diagnosis is awareness of the condition. If the disorder is not considered, it will certainly not be recognized. As always, a careful history is also of paramount importance. Every patient with indeterminate pulmonary disease should be closely questioned with reference to the habitual use of oily nose drops or mineral oil at any period of his life. If an affirmative history is obtained, the sputum should be studied for the presence of oil droplets. When this examination is positive and the roentgenogram reveals bilateral pulmonary lesions,

the diagnosis of lipoid pneumonitis can be accepted with reasonable certainty—particularly if the pulmonary changes are known to have been present for a long period. If the lesion in question is solitary and circumscribed, however, and the duration of the disease is unknown, the diagnosis becomes somewhat less certain since the history of use of oily materials, and even the demonstration of oil droplets in the sputum, fails to afford absolute evidence that the patient does not have pulmonary neoplasm. In such cases the diagnosis may be strongly suspected but resection of the lesion will frequently be indicated both from a diagnostic and a therapeutic standpoint. In other cases, the history may be uncertain and oil droplets are hardly likely to be demonstrated many years after the aspiration of the offending agent has been discontinued, or if the oil is completely trapped within the lung by bronchial obstruction. In these instances the physician is faced with a truly indeterminate lesion which cannot be differentiated from bronchogenic carcinoma. Exploratory thoracotomy then becomes mandatory and frozen section is imperative since the granuloma may continue to masquerade as a neoplasm even on gross inspection and palpation, and may result in needless sacrifice of pulmonary tissue if its true identity is not immediately established. When the disease is localized and unilateral, resection of the involved lobe or segment is curative.

Case 1: A. E., a 45 year old white male, superintendent of a manufacturing plant, was admitted to the hospital on January 19, 1949, as a referral from his private physician for consideration of lobectomy for "bronchiectasis with superimposed, intractable pneumonitis." History disclosed that he had been troubled with chronic sinusitis for 20 years. This condition was associated with chronic post-nasal drip and cough productive of moderate amounts of thick mucoid sputum of a mucopurulent character. In July, 1948, he vacationed in the San Joachim valley in California. A week later he developed nonsuppurative otitis media, which was treated with a sulfa preparation. This medication caused a febrile reaction and desquamating dermatitis. Following recovery from this complication he complained only of easy fatigability and sporadic cough, until December 1, 1948, when he began to expectorate liquid and clotted blood in two to three ounce quantities. He was admitted to a private hospital where a roentgenogram of the chest disclosed a circumscribed area of infiltration in the right lower lobe, which had also been present on a previous routine pre-employment roentgenogram of February 26, 1947. Hemoptysis continued to occur several times each day, and on December 18, 1948, dihydrostreptomycin therapy was instituted. Two days later, hemoptysis ceased and did not recur. Bronchoscopy and bronchography were carried out. Lipiodol failed to fill the right middle and lower lobes, and a tentative diagnosis of bronchiectasis with chronic pneumonitis was proposed. Surgical intervention was not felt to be indicated at that time and he was released from the hospital. When subsequent observation failed to disclose change in the roentgenographic findings, he was advised to enter the veterans hospital for consideration of lobectomy.

Physical Examination: He was a well-developed, slightly obese white male, who did not appear to be ill. The temperature was 98.6° F. the pulse 78, and the blood pressure 108/68. Both tympanic membranes were retracted; the right was markedly reddened. The nasal mucosa was boggy and injected; septal spurs were present bilaterally. Examination of the thorax revealed bilateral gynecomastia. Slight hyperresonance was noted over the lower one-third of the right lung field and occasional musical rales were present in this area. Small non-tender lymph nodes were palpated in the posterior cervical region and in both axillae.

Laboratory Studies: Roentgenograms of the chest revealed an irregular

FIGURE 1

FIGURE 2

FIGURE 3

Figure 1 (Case 1): Erect postero-anterior roentgenogram showing an irregular density in the right paracardiac area.—*Figure 2* (Case 1): Body section roentgenogram showing a lesion in the left retrocardiac area in addition to the previously visualized right paracardiac density.—*Figure 3* (Case 1): Bronchogram in right anterior oblique projection demonstrating obstruction of a segmental bronchus of the left lower lobe at the superior portion of a circumscribed pulmonary nodule.

density in the right paracardiac area and a previously undetected density in the left retrocardiac region (Figures 1 and 2). A review of his service roentgenograms disclosed that the density in the right lung had been present without significant change since December 16, 1942. Serological test for syphilis, complete blood count and urinalysis were normal. Multiple sputum examinations were negative for acid-fast bacilli and neoplastic cells. Tuberculin skin test with first strength PPD was 2-plus. A skin test with coccidioidin in dilution of 1:100 was 1-plus. Histoplasmin skin test was negative. A G.I. Series, barium enema and I.V. pyelogram were essentially normal. Bronchoscopy on February 2, 1949, disclosed no abnormality of the trachea, carina or the right bronchial tree. However, the mucosa of the left lower bronchus was injected and hypertrophied just below the orifice to the upper lobe. A biopsy from this region was reported as showing slight chronic inflammation with minimal squamous metaplasia. Cultures of bronchial washings were negative for acid-fast bacilli. Lipiodol instillation into the tracheobronchial tree outlined all lobes. No abnormality of the right upper or middle lobes could be detected. Slight beading of a few of the smaller bronchial branches of the right lower lobe suggested minimal bronchiectatic changes but there did not appear to be any communication between the bronchi and the paracardiac mass. The left bronchial tree was normal with the exception of one branch of the lower lobe bronchus which appeared to be completely occluded at a point corresponding to the superior portion of the retrocardiac mass (Figure 3).

Hospital Course: Additional history revealed that he had habitually used oily nose drops for the relief of symptoms related to chronic sinusitis during the 10-year period from 1933-1943. Unfortunately, this information did not prompt examination of the sputum for oil droplets, but considerable emphasis was placed on a diagnosis of lipoid granuloma. Several observers, however, felt that coccidioidomycosis or primary or metastatic neoplasms should be considered, and exploratory thoracotomy was advised. Because of evidence of occlusion of a segmental bronchus in the left lower lobe, this area was chosen for exploration. On March 2, 1949, left thoracotomy was carried out. A firm, nodular mass was encountered in the medial aspect of the lower lobe and the lobe was resected. Dissection of the surgical specimen disclosed stenosis and occlusion of the anterior basal segmental bronchus at a point 3.5 cm. from its origin. Beyond this point the bronchus was completely destroyed and entered a yellowish-gray nodule which measured 3.5 cm. in diameter. Histological study established a diagnosis of lipoid granuloma (Figure 4). The postoperative course was uncomplicated and he was discharged from the hospital on March 18, 1949.

Comment: In retrospect, it would appear that exploratory thoracotomy for diagnostic reasons alone was unnecessary in this case. The history of habitual use of oily nose drops over a period of 10 years, together with the demonstration of bilateral lower lobe densities which had not changed significantly in more than six years, was certainly evidence

enough to establish a diagnosis of benign disease probably due to aspiration of oil. If, in addition, the sputum had been examined for oil droplets and their presence demonstrated, the diagnosis of lipoid granuloma might have been accepted with reasonable certainty. Surgical intervention would then have been indicated only as a therapeutic measure.

Case 2: J. P., a 58 year old white male farmer, was admitted to the hospital on November 11, 1949, as a transfer from another institution for the treatment of "possible malignancy of the right middle lobe." History revealed that for the past seven years he had complained of intermittent episodes of cramping sub-sternal pain accompanied by dyspnea. About four years prior to admission, he developed chronic cough productive of small amounts of greenish sputum and associated with dull pain in the right lower anterior chest. Gradual weight loss of 15 pounds had occurred. Because of progression of the above symptoms he finally consulted his private physician and was referred to veterans administration hospital. Roentgenograms revealed a solid density in the right middle lobe, he was considered to have probable broncho-

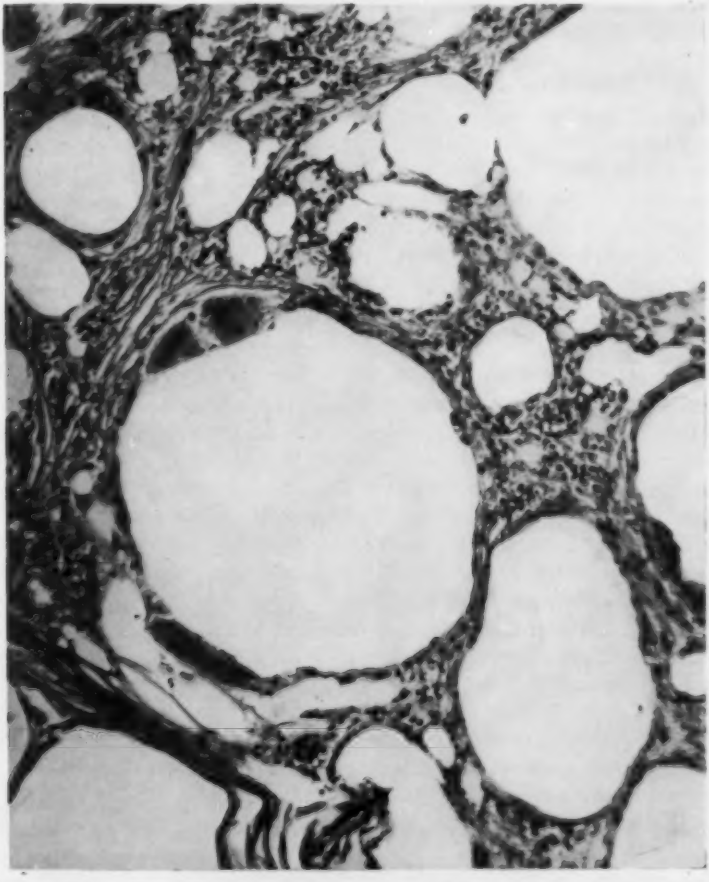

FIGURE 4 (Case 1): Photomicrograph of tissue section stained with hematoxylin and eosin, showing tissue spaces which contained oil. Note presence of foreign body giant cells lining large central oil spaces.

genic carcinoma, and was transferred to the New Orleans hospital for further management.

Physical Findings: He was a well-developed, moderately nourished white male who appeared to be chronically ill. The temperature was 98.6° F. pulse 82, and blood pressure 130/80. Examination of the chest revealed diminished breath sounds together with decreased resonance and tactile fremitus over the right lower lung field posteriorly. The remainder of the physical examination was not remarkable.

Laboratory Studies: Roentgenograms of the chest disclosed a triangular density which appeared to occupy the entire extent of a contracted right middle lobe, with associated slight elevation of the right hemidiaphragm (Figure 5). Complete blood count was within normal limits except for slight leukocytosis of 11,650 and eosinophilia of 6 per cent. Serology and urinalysis were normal. One of many sputum concentrates was positive for a "few acid-fast organisms." Gastric washings were negative for acid-fast bacilli. Sputum examinations were repeatedly negative for fungi and malignant cells. Stools were positive on several occasions for trophozoites and cysts of E. Coli and E. Nana and cysts of E. histolytica. Culture for E. histolytica was also positive. Gastrointestinal series revealed a zone of narrowing in the pyloric end of the stomach near the pyloro-duodenal junction. The duodenal cap was constantly deformed and a prestenotic diverticulum was noted at the base of the bulb. The radiologist's impression was ulcer of the duodenum. Tuberculin tests in first and second strength, histoplasmin test, and coccidioidin test were negative. Bronchoscopy revealed no abnormality other than a small amount of mucopurulent secretion in the right bronchial tree. Cultures of these secretions for acid-fast bacilli and cytological studies for malig-

FIGURE 5

FIGURE 6

Figure 5 (Case 2): Erect postero-anterior roentgenogram showing opacification of the right middle lobe.—*Figure 6* (Case 2): Bronchogram in lateral projection demonstrating complete occlusion of the right middle lobe bronchus.

nant cells were negative. A bronchogram demonstrated complete obstruction of the right middle lobe bronchus at a point approximately 2 cm. from its origin (Figure 6). No other significant abnormality was observed. Four consecutive sputum specimens were found to contain a few oil globules when examined with fat stains.

Hospital Course: Subsequent history disclosed that the patient had for many years indulged in the practice of deliberately aspirating mineral oil in the belief that it had a beneficial effect on minor respiratory infections. After this history was obtained, the sputum was studied for fat droplets, with positive results. A diagnosis of lipoid granuloma of the lung was then given strong consideration, but it was felt that the presence of bronchogenic carcinoma could not be absolutely ruled out and exploratory thoracotomy was recommended. On February 17, 1950, the middle lobe of the right lung was resected with great difficulty because of the presence of dense pleural adhesions which had obliterated the pulmonary fissures. While carrying out the dissection of the middle lobe, a cavity was entered from which about 10 cc. of yellow, oily material escaped. The lining of this cavity was composed of necrotic, cheesy material. A portion of the cavity wall was sent to the laboratory for frozen section but the pathological study was reported as inconclusive. It was the surgeon's impression, however, that the disease process was not malignant and that lobectomy alone was indicated. Attempts to isolate the pulmonary vein to the middle

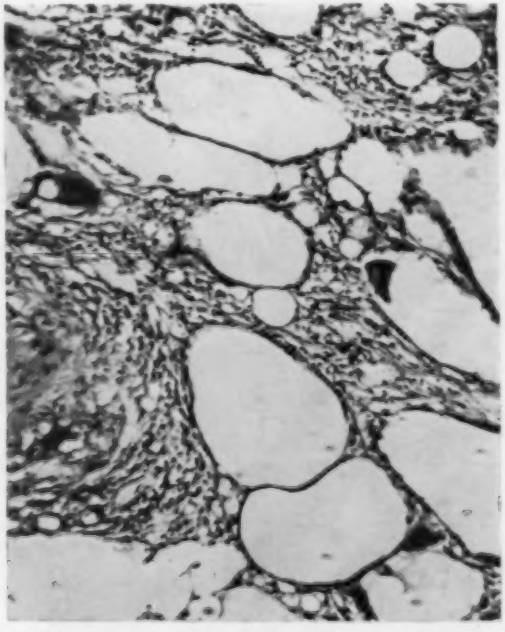

FIGURE 7 (Case 2): Photomicrograph of tissue section stained with hematoxylin and eosin. Scattered giant cells, an area of granulomatous reaction and many oil spaces are demonstrated.

lobe were unsuccessful and the lobe was finally removed by amputation near the hilus. The postoperative course was essentiallly uneventful and he was discharged from the hospital on March 24, 1950. Histological study of the resected lobe established a diagnosis of "lipoid granuloma" (Figure 7).

Comment: Proper evaluation of the patient's history and examination of the sputum for oil content resulted in a correct preoperative diagnosis of lipoid granuloma in this case. However, the presence of a unilateral lesion of unknown duration associated with complete occlusion of a major bronchus still suggested the possible existence of a bronchogenic carcinoma, which could not be excluded by any diagnostic method other than exploratory thoracotomy. This procedure confirmed the diagnosis and the accompanying lobectomy resulted in a cure of the patient.

Case 3: C. Y., a 56 year old white male narcotic addict and professional hospital inhabitant was admitted to the hospital on October 14, 1953, as a direct transfer from another institution for further evaluation of a pulmonary lesion regarded as a probable bronchogenic carcinoma. History disclosed that he had been hospitalized on 35 previous occasions since 1922 for a variety of illnesses including otitis media, bronchitis, appendicitis, tonsillitis, gunshot wound of right knee, mental deficiency, ankylosis of the right knee, chronic osteomyelitis of the right knee, amputation of the right leg, narcotic addiction, painful amputation stump, cholecystitis, cholecystectomy, recurrent obstruction of the common bile duct, postoperative ventral hernia, multiple skin abscesses, and constitutional psychopathic state. On September 25, 1953, he was admitted to a hospital for the 36th time complaining of severe epigastric pain, right upper quadrant pain, nausea, vomiting, black stools, headache, joint pains, and painful amputation stump. He had been taking 150 or more ½ grain morphine tablets weekly until three weeks prior to admission to the hospital. Since that time, he had been unable to obtain further narcotics and it was strongly suspected that withdrawal of drugs constituted the main basis for his complaints. No respiratory symptom was present. Routine roentgenogram of the chest disclosed an area of infiltration in the base of the right

FIGURE 8 (Case 3): Erect postero-anterior roentgenogram showing area of infiltration in base of right upper lobe.

upper lobe which suggested the presence of bronchogenic carcinoma. Transfer to the hospital at New Orleans was then recommended.

Physical Findings: He was a dirty, disheveled, right-leg amputee who did not appear to be ill but who sat in a wheelchair and complained bitterly of right upper quadrant pain. He gave a contradictory history, the facts of which were at considerable variance with his previous records. The temperature was 98.6° F., pulse was 72, and blood pressure was 125/88. Pupils were pin-point and exhibited no reaction to light. Innumerable small punctate scars and nodular erythematous lesions were scattered over the skin of the arms, anterior chest, shoulders, and thigh of the left leg—apparently indicating the infected sites of multiple hypodermic injections. There was induration of the veins of both antecubital fossae. Multiple surgical scars were present on the abdomen and there was tenderness and voluntary guarding in the right upper quadrant. The right leg had been amputated at mid-thigh. The stump was well-healed and nontender. Examination of the chest disclosed no significant abnormality.

Laboratory Studies: Roentgenograms of the chest disclosed an area of calcification in the right hilum with peripheral contraction and infiltration of the anterior segment of the right upper lobe (Figure 8). Body section planigrams demonstrated the calcium within a node adjacent to the inferior border of the right upper lobe bronchus in the region of origin of the anterior segment. Bronchogram detected no significant abnormality. On bronchoscopy, the trachea was deviated to the left; the posterior wall bulged inward slightly at a point corresponding to the aortic arch. The carina was thickened and set at an angle of 70 degrees to the right. There

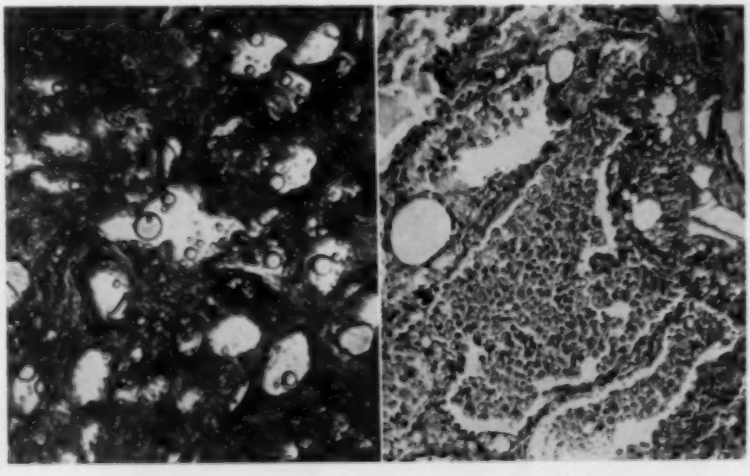

FIGURE 9 FIGURE 10

Figure 9 (Case 3): Photomicrograph of tissue section stained with Oil red O. Note the presence of numerous oil droplets which, when seen in color, appear bright yellow against a tissue background of brilliant blue.—*Figure 10* (Case 3): Photomicrograph of tissue section stained with hematoxylin and eosin demonstrating alveolar spaces filled with oil containing macrophages.

was some edema of the inferior lip of the right upper lobe orifice, and biopsy was taken at this point. No other abnormality of the bronchial tree was noted. Biopsy tissue was inadequate for diagnosis. Multiple sputum examinations were negative for acid-fast bacilli and malignant cells. A test with first-strength tuberculin was one-plus. Histoplasmin test was two-plus. Coccidioidin test was negative. Complete blood count and urinalysis were normal. Several stool specimens were reported as containing much oil. The sputum was not examined for oil content.

Hospital Course: A review of his previous roentgenograms disclosed that the lesion in the right lung had been present since November, 1948, although it was much smaller at that time. On the basis of this information and the association of a calcified hilar node to the contracted segment of the right upper lobe, a tentative diagnosis of broncholithiasis with secondary inflammatory changes was proposed. Intensive therapy, which included penicillin, streptomycin, terramycin and triple sulfa, failed to produce significant benefit, and by January, 1954, a sudden increase in the extent of the pulmonary lesion prompted consideration of the possibility that bronchogenic carcinoma might be present in spite of the known duration of the disease process. Exploratory thoracotomy was advised. On January 13, 1954, the chest was entered and a "firm, cobblestone tumor mass" was found in the anterior segment of the right upper lobe and the lobe was resected. On cut surface, the nodule presented a greasy yellowish appearance, and frozen sections established a diagnosis of "lipoid granuloma" (Figures 9 and 10). After the nature of the pulmonary lesion had been established by the pathologist, the patient was questioned for the first time with reference to the possible aspiration of oily materials. He had used mineral oil habitually for many years and stated that he would frequently "gag" on dry foods and occasionally with liquids. On these occasions he would feel as though the food or liquid "had gone down the wrong way." A review of his previous hospital records indicated that mineral oil had frequently been prescribed since 1935, and indeed its use had been continued during the present period of hospitalization while attempts were being made to establish the etiology of the pulmonary disease. The postoperative course was uneventful and he was discharged from the hospital on February 2, 1954.

Comment: In this case the correct diagnosis was not given even remote consideration prior to surgery and came as a complete surprise when the report of frozen section was received. Had an awareness of this condition existed, had it been included in the differential diagnosis, and had the patient been questioned with reference to the possible aspiration of oil, as should have been done, at least a clue to the presence of lipoid granuloma would have been obtained. Had oil droplets then been demonstrated in the sputum, the diagnosis might have been accepted without great reservation since the lesion was known to have been present for five years. It is interesting to speculate on whether the progression of the disease process, which occurred while he was under observation, was due to continued administration of mineral oil during that time.

SUMMARY AND CONCLUSIONS

1. Lipoid granuloma of the lung of exogenous origin is still encountered with some frequency and is almost as often misdiagnosed, largely because it is not considered in the differential diagnosis of obscure pulmonary lesions.

2. Diagnosis can be made with reasonable assurance in many cases where bilateral lesions are present if the physician is aware of the condition, takes a careful history with reference to possible aspiration of oily materials and examines sputum specimens for oil content.

3. Circumscribed unilateral lesions may closely mimic bronchogenic carcinoma and will frequently require exploratory thoracotomy for confirmation.

4. Frozen section should always be obtained in order to avoid needless sacrifice of pulmonary tissue.

5. Resection is curative when the disease is localized and unilateral.

RESUMEN Y CONCLUSIONES

1. El granuloma lipóidico del pulmón de origen exógeno, se encuentra aún con alguna frecuencia y es lo más a menudo mal diagnosticado, principalmente porque no es considerado en el diagnóstico diferencial de las lesiones pulmonares obscuras.

2. El diagnóstico puede hacerse con relativa seguridad en muchos casos en que hay lesiones bilaterales si el médico tiene presente esta afección, hace una historia cuidadosa en lo relativo a posible aspiración de materiales aceitosos y examina los esputos buscando el aceite.

3. Las lesiones unilaterales circunscritas, pueden muy estrechamente asimilarse al carcinoma bronquigénico y frecuentemente se requerirá la toracotomía exploradora para la confirmación.

4. Se deben obtener siempre cortes congelados para evitar el sacrificio inútil de tejido pulmonar.

5. La resección es curativa cuando la enfermedad es unilateral y localizada.

RESUME

1. Les tumeurs lipoïdes du poumon d'origine exogène sont encore rencontrées avec quelque fréquence et sont assez souvent mal diagnostiqués, pour une grande part parce qu'elles n'entrent pas en considération quand on envisage le diagnostic différentiel des lésions pulmonaires de nature inconnue.

2. La diagnostic peut être fait avec certitude dans beaucoup de cas où il existe des lésions bilatérales, si le médecin est au courant de ces état, relève minutieusement l'histoire, avec indication d'une éventuelle absorption de produits huileux, et examine les produits d'expectoration pour la recherche du contenu huileux.

3. Les lésions unilatérales circonscrites peuvent suggérer de très près un cancer bronchique et nécessiteront fréquemment une thoracotomie exploratrice pour le confirmer.

4. La biopsie extemporanée devrait toujours être pratiquée pour éviter un sacrifice inutile de tissu pulmonaire.

5. La résection est curative quand l'affection est localisée et unilatérale.

SCHLUSSFOLGERUNG

1. Ein Lipoid-Granulom der Lunge exogenen Ursprungs wird immer mit einiger Häufigkeit auftreten und oft fehlgedeutet, besonders weil es bei der Differentialdiagnose unklarer Lungenherde nicht in Erwägung gezogen wird.

2. Die Diagnose kann in vielen Fällen mit einiger Sicherheit gestellt werden, in denen bilaterale Herde bestehen, wenn der Arzt die Krankheitsumstände kennt, eine sorgfältige Vorgeschichte aufnimmt mit Bezug auf mögliche Aspiration von öligem Material und Auswurfpräparate auf ihren Ölgehalt prüft.

3. Umschriebene einseitige Herdbildungen können ein bronchogenes Carcinom täuschend nachahmen und werden häufig eine diagnostische Thorakotomie zur Bestätigung notwendig machen.

4. Einen Gefrierschnitt muss man immer gewinnen, um ein nicht notwendiges Opfer von Lungengewebe zu vermeiden.

5. Die Resektion bedeutet die Heilung, wenn die Erkrankung lokalisiert und einseitig ist.

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Non-Specific Infections in Diseases of the Lungs and Bronchostenosis

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For more than 10 years now, systematic investigations pertaining to non-specific infections have been in progress at St. Göran's Sjukhus, and in the course of the years 50-odd papers have been publicised on clinical, patho-anatomical, experimental, serological and bacteriological observations.[1-6, 11-16, 18] The major proportion of the patient material, at present amounting to at least 8,000 cases, consists of all forms of pulmonary tuberculosis, as well as pleurisy and erythema nodosum, but all kinds of diseases affecting the internal organs, including non-tuberculous pulmonary conditions, have also been analysed.

Briefly put, these studies disclosed that active, non-specific infections—of an acute and, still more, chronic nature—occur to an extent which formerly had scarcely been realized. As indices of such an infective influence were in all cases chiefly studied the serum titres, in the first place those of antistreptolysin (AS) and antistaphylolysin (ASta). However, direct, bacteriological tests during life and after death were also performed, as were experiments with animals, etc., the results on the whole showing fair agreement with those of the titre determinations. Of course, the AS titre merely indicates systemic impairment by β-haemolytic streptolysin-producing streptococci and the ASta titre that due to yellow α-staphylolysin-producing staphylococci. It cannot be doubted that there are many more types of pathogens which give rise to non-specific infections to the same, or surely to even a greater extent than the two just mentioned, allowing demonstration by means of dependable and convenient serological methods. (In roughly 1,500 cases the agglutination of *Esch. coli* was also investigated and similar titre rises were observed.[12]) Hence, the incidence rates of titre elevation within the various morbid groups as given in the present paper, to a certain degree (but naturally to a certain degree only) may be regarded as indicators of the occurrence of active, non-specific infections altogether—This, however, should by no means be taken to imply any doubt as to the specificity in respect of the streptococci and staphylococci just mentioned—It is greatly to be regretted that there are no sufficiently convenient and reliable methods of demonstrating the influence of other non-specific pathogens, such as non-haemolytic streptococci and many others.

As titre rises were regarded, for AS rates of 200 units or more, and for ASta 1.4 units or more. These figures cannot claim to be more than sorting-out limits suited to practical conditions. It might well be justified to put the limits somewhat lower (or even higher), but in surveys of large series the differentiation between "normal" and "pathological"

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would hereby apparently become less illuminating. In "healthy" subjects not infrequently titre rates are found which exceed the above limits, and even though a series of "healthy" persons be minutely cleared of everything possibly suggesting, on clinical grounds, infections etc., still at least about ten per cent of the subjects must be expected to present titre rates above the limits just mentioned. This applies largely to materials from the Scandinavian countries. At least as regards infection by haemolytic streptococci, this seems to be more common here than e.g. in Great Britain and the United States, where lower incidence rates have been noted in normal series. (Possibly this observation might imply that the incidence of titre rises in diseases of various kinds may also be higher in our countries than in many other parts of the world.) The significant fact that older persons on an average show lower rates of titre rises than younger subjects[12] may be considered irrelevant to the results presented in this paper, which is still more true of a slight sexual difference emerging from the present survey (somewhat higher rates for younger men *versus* younger women, especially as regards the AS titre, and somewhat higher rates for older women *versus* older men in respect of the ASta titre).

A comparison of the titre rates in various types of tuberculosis cases soon disclosed that patients with symptoms of bronchostenosis strikingly often had raised titres[12, 14] which was confirmed by further analysis of the material.

Lymph Node Perforations, Bronchial Stenosis and Allied Conditions.

Very likely several different factors are involved in the pathogenesis of bronchial obstruction in cases of tuberculosis, but no doubt most important are *inflammatory processes in adjacent lymph nodes and reparative phenomena associated with them.* Perforation processes arising from tuberculous intrathoracic lymph nodes have in fact been well known since long ago, at least from the standpoint of morbid anatomy, and occasional clinical observations have also been on record for several decades. Such perforation processes may develop in many directions, among which, by the way, here only perforation into the oesophagus may be mentioned, the course of which practically always seems to lack alarming symptoms, even its better known sequelae, the traction diverticula, will but rarely give rise to clinical signs.[17] Much more common, and of far greater practical importance, is perforation from tuberculous lymph nodes into adjacent bronchi, and of recent years, not least after the work done by Schwartz, more attention has been paid to this occurrence.

I have been keenly interested in the relevant problems for more than 20 years, though earlier my opinions on this subject were given merely in the form of some brief notes.[7, 10] In the present paper I will chiefly put forth the following thesis. (In the discussion on perforations of intrathoracic lymph nodes these phenomena have not received much consideration.) *The most important cause of perforations or special encircling irritation altogether emanating from the tuberculous lymph nodes, is a clash in the latter between a tuberculous process and one or several non-specific infections.* About 1937 I coined the catchword, "Multiple

infections will explode the tuberculous lymph node.[9]" In tuberculous lymph nodes of the neck perforations often develop after ordinary pharyngitis, and similar factors must be still more important where the pulmonary nodes are concerned.

One chief item connected with this matter must be *bronchostenosis*. Most of the perforation processes arising from pulmonary lymph nodes apparently heal very soon, and it may be rather difficult, if not impossible, to demonstrate them later on. In many cases, however, the inflammatory irritation emanating from the lymph node will continue and be followed by chronic alteration of the bronchial wall, and more or less marked narrowing of the bronchial lumen may develop. On a cicatricial basis inflammatory oedema, transient or long-standing, is often superimposed, whereby the narrowness is increased. Similar processes in the bronchial wall may admittedly be due also to invasive periadenitis without any perforation proper. In cases of pulmonary tuberculosis bronchostenosis is well known nowadays, and this phenomenon is undoubtedly of eminent pathogenetic and clinical significance.

However, constriction processes, as a rule very slight, are not infrequent even in cases without any known preceding (or subsequent) tuberculous disease, and where the pulmonary radiograms, etc., fail to disclose any appreciable evidence of tuberculous lesions. This, as a rule, must be a consequence of residues left by subsiding, long ago healed, central tuberculous involvement, not least of those derived from the primary stage of tuberculosis (during which, in the light of present knowledge, the incidence of perforating processes is rather high) together with acute or chronic, non-specific infective agencies.

Increase of Serum Titres in Different Types of Pulmonary Diseases

In Table I, is presented clinical material including, on the one hand, three main groups of tuberculosis patients of 911, 4,072, and 957 cases respectively, and, on the other, in all 825 cases of non-tuberculous pulmonary diseases (without any noteworthy tuberculous disease past or present), divided into four main groups.

The first column in the table then pertains to the incidence of raised AS and ASta titres respectively within each of these main groups. Now, we find high rates for the tuberculosis cases; special attention should be paid to the fact that the pleurisy group shows about the same incidence rates as the cases of pulmonary tuberculosis proper; 46.5 per cent of the 911 patients with acute pleurisy, i.e. 424 subjects, presented AS rises during the first two months following the onset of disease, and ASta elevation was noted in 43.1 per cent, whereas the corresponding incidence rates are 47.7 per cent respectively 40.4 per cent for the entire material of pulmonary tuberculosis proper (whether mild or grave). In this second group of the table no conditions involving acute pleurisy are included, nor those that were referred to the third group: patients whose morbid process could be considered healed or relatively so. As to the latter group, we find that titre elevation occurs to a clearly less extent (for AS in 35.5 per cent, respectively, for ASta, in 26.4 per cent of the cases) but these latter

TABLE I

Percentages of Positive Antistreptolysin (AS) and Antistaphylolysin (ASta) Titres in Relation to Bronchostenosis

		No. of Cases	AS ≧ 200	ASta ≧ 1.4	Symptoms of Stenosis	No. of Cases	AS	ASta
Tuberculosis	Acute Pleurisy	911	46,5	43,1	neg	667	40,8	40,4
					pos	244	62,3	49,5
	Pulmon. Tuberc.	4072	47,7	40,0	neg	2791	39,7	32,3
					pos	1281	65,1	53,8
	D:o, "Healed"	957	35,3	26,4	neg	704	32,4	22,4
					pos	253	43,5	36,5
Non-Tuberc. Pulmon. Conditions	Various Acute	352	40,1	31,7	neg	310	38,4	31,8
					pos	42	52,4	30,0
	Various Chronic	180	35,0	35,0	neg	152	31,6	34,1
					pos	28	53,6	39,3
	Bronch. Asthma	202	20,8	17,9	neg	193	19,7	17,3
					pos	9	44,4	33,3
	Pulm. Carcinoma	91	21,9	19,2	neg	36	8,3	12,0
					pos	55	30,9	23,5

incidence rates are nevertheless about three times higher than those observed in a "normal" series.

In the lower portion of the table are then arranged four groups of non-tuberculous pulmonary diseases showing incidence rates of titre rises of about the same order of magnitude as in the cases of "healed" tuberculosis just mentioned. When the group, various acute conditions, (chiefly different types of acute pneumonia) is compared with the next group, various chronic conditions, the somewhat higher AS figure in the former (40.1 per cent as against 35.0 per cent) and the somewhat higher ASta figure in the latter (35.0 per cent as against 31.7 per cent) might deserve attention.

In the asthma cases and also in the cases of pulmonary carcinoma we find incidence rates of a totally different order of magnitude. The on an average low serum titres in these groups are striking already on comparison with the just mentioned groups of various acute respectively chronic pulmonary conditions and still more so on comparison with the tuberculosis cases. Clinically, infective processes, especially acute and chronic bronchitis, are very common among these asthma patients (on an average it is here a question of comparatively grave, chronic cases with more or less pronounced pyrexia in the major proportion of instances), and as regards the carcinoma cases the hazard of supervening, non-specific bronchitis ("secondary infections") might even be considered higher than in any other group of the entire table. Possibly some kind of cachexia-anergetic factor, causing reduced titre rises, may be suspected in the carcinoma cases (true, clinical cachexia, however, had developed in but few of them). In respect of the asthma cases, on the other hand, no similar explanation is possible. At an earlier date I have emphasized that although asthma patients certainly to a great extent must be regarded as "infection-sensitive," their resistance to infections, as regards septic conditions more serious in

type, on the whole can be deemed good. One might say that in the asthmatic (allergic) the mechanism intended to counteract infective damage runs with much clanking and disturbance, but that after all its efficaciousness is as a rule well maintained. In my opinion the average low serum titres of asthma patients should be considered to represent constitutional features, in particular those bearing upon resistance to infections. The low titres presented by these patients (and the same could be presumed concerning the relatively low titres frequencies in old people) should not be interpreted as a sign of failing reactivity comparable to cachexia, but as a manifestation of the fact that these subjects *do not need* the quantitatively powerful mobilization of defense against septic infections which is the rule in e.g. tuberculosis cases.

The disadvantage of the tuberculosis patient in this respect, viz. their generally poor resistance to infections, has actually been known from over-all clinical experience since long ago, and one has spoken of "mixed" or "secondary" infections, etc. However, it must be forcefully stressed that the indices of supervening non-specific infections which these titre rises furnish, are *not* (or only to a very slight degree) attributable to such secondary processes (more on this point will follow lower down in the present paper).

TABLE IIA

Relation between incidence of raised AS and ASta, resp., during 6 months preceding post mortem, and growth of resp., bacteria

	Negat. (or superfluous, resp.)	Posit. (or deep, resp.)
AS $\gtrless$ 200	18,8 per cent	70,0 per cent
ASta $\gtrless$ 1,4	c. 17 per cent	c. 53 per cent

TABLE IIB

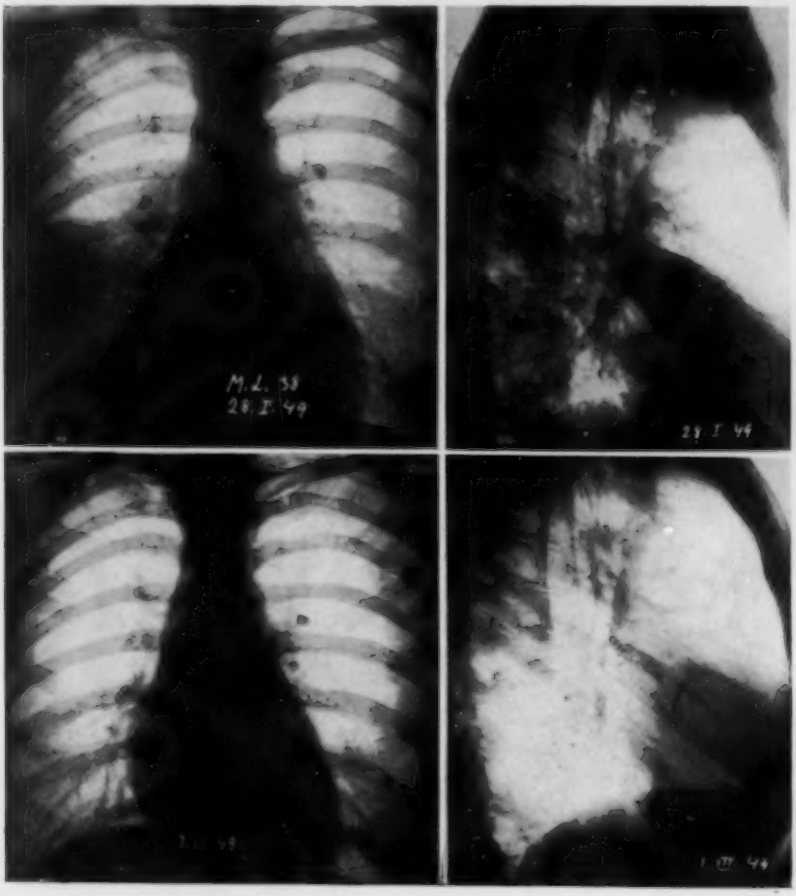
Occurrence post mortem in lymph nodes of β-hemolytic streptococci and yellow staphylococci, resp., in various clinical groups

	Respir. syst.		Abdomen		Spleen	
	Strept.	Staph.	Strept.	Staph.	Strept.	Staph.
No infectious disease	5,6	19,5	4,3	3,6	6,5	7,0
Infections (not pulmonary)	29,4	47,5	25,0	37,5	25,0	31,2
Pulmonary infectious disease (non-tub.)	12,5	62,5	0	20,0	9,1	36,3
Cases of tuberculosis	27,0	81,1	9,4	46,9	10,7	53,6

Even if the specific nature of AS and ASta, respectively, is fully accepted, this of course cannot be taken as a declaration that in the cases with "positive" serum titres in Table I the patient's lungs or his pulmonary and mediastinal lymph nodes are invaded by haemolytic streptococci or yellow staphylococci. However, Adamson's[1] bacteriological investigations on autopsy material seem to be of a special value for illustrating these problems. In Adamson's study all bacteria demonstrated in the lymph nodes are included, but here only a short summary shall be given with reference to haemolytic streptococci and yellow staphylococci. Table IIA shows a fairly close agreement between the findings of haemolytic streptococci and the patient's antistreptolysin titre, and a somewhat looser, though fully obvious, agreement between yellow staphylococci and the antistaphylolysin titre. Table IIB in particular discloses that a positive

culture test of these bacteria is more common throughout within the lymph nodes of the respiratory tract than in the abdominal lymph nodes or in the spleen, but it will be seen in addition, that the tuberculosis cases altogether present a higher incidence of bacterial findings than other clinical groups. (The high rates of streptococcal findings in the second clinical group of Table IIB—Infections—are due to the group including cases of frank septicaemia). Within all lymph-nodes groups the tuberculosis cases (with the same exception as that just mentioned) display higher incidence rates than the cases of the three other clinical groups, and the highest rates in Table IIB relate to the lymph nodes of the respiratory tract in the tuberculosis cases, where haemolytic streptococci were found in 27 per cent and yellow staphylococci in no less than 81 per cent.

Thus the highest incidence of positive growth was found in the lymph nodes of the respiratory system of such cases where in my opinion the multiple infections are of the greatest importance, and, as was emphasized earlier in this paper, such infections must be regarded as a highly important pathogenetic factor in the origination of glandular perforation, and also of bronchostenosis.

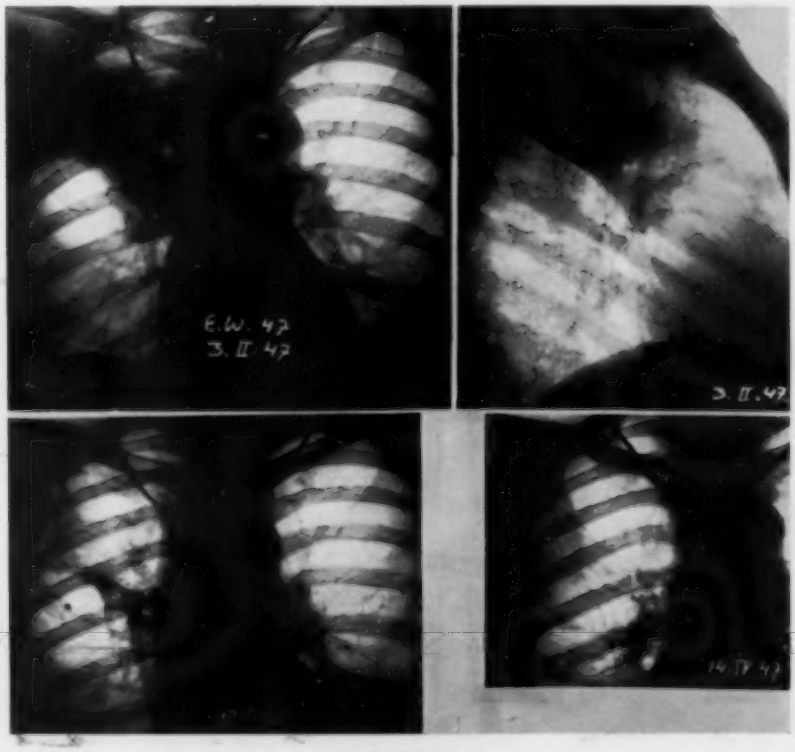


CASE 1

Serum Titres in Relation to Bronchostenosis.

We revert to Table I. In the last four columns the clinical groups are subdivided in such a manner that all cases where symptoms of bronchostenosis had not been recorded ("neg.") were separated from the cases where during some period of their histories roentgenologically and/or bronchoscopically more or less pronounced phenomena of bronchostenosis could be considered definitely proved or highly probable ("pos."). Among the non-tuberculous cases, however, bronchoscopy was carried out only where there were special reasons to suspect processes of this type (thus e.g. in practically all cases of pulmonary carcinoma), but otherwise only in comparatively few instances, whereas the major proportion of tuberculosis patients, especially during the last five years, have been examined bronchoscopically. Also transient signs of stenosis, in which acute inflammatory factors had participated, were recorded (though not occasional phenomena of this type, e.g. after an haemoptysis).

As we find in the table, all three groups of tuberculosis cases have both incidence rates of titre rises much higher in the stenosis cases than in the remaining ones. Within the respective groups, all differences between stenosis cases and those without stenosis are statistically strongly supported

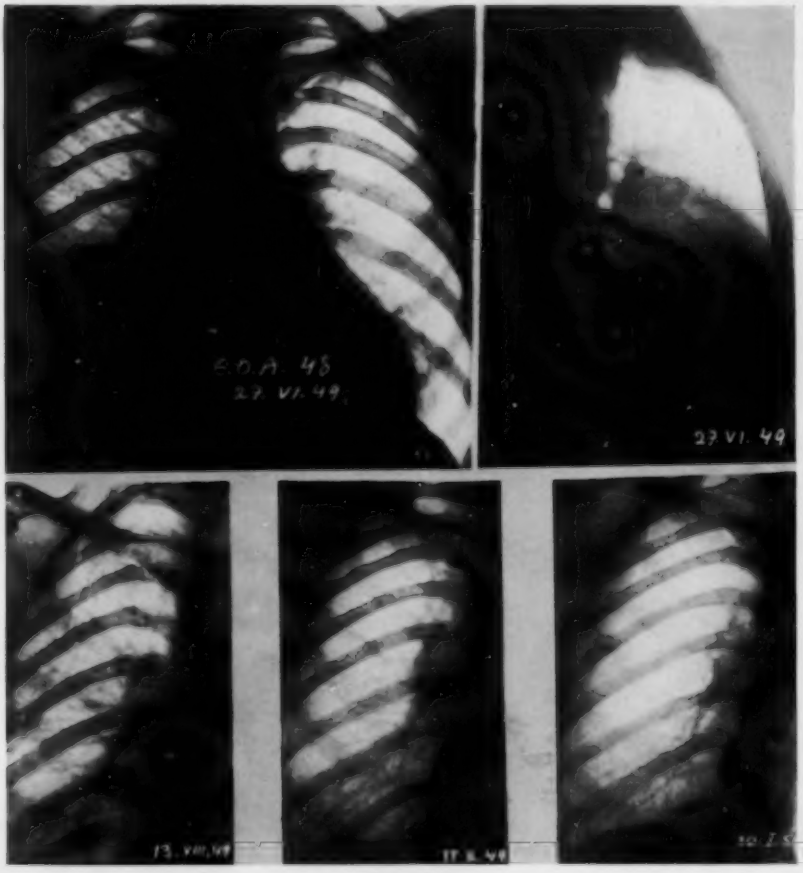


CASE 2

as regard both AS and ASta. The same tendency is also apparent for the four separate groups of non-tuberculous conditions, the most marked differences being noted in the asthma group and the carcinoma group. (Owing to the smaller materials, however, statistical support is uncertain.) The observations just mentioned of higher incidences of titre elevations in non-tuberculous cases with signs of stenosis might possibly be taken to indicate a more powerful effect of infective processes in bronchiectasis or, generally speaking, of retained infections, especially as regards asthma and carcinoma cases. As suggested just now, however, a corresponding pathogenetic mechanism on the whole cannot be of importance where the tuberculosis cases are concerned.

Serum Titres and Bronchostenosis in Relation to Degree of Pulmonary Tuberculosis

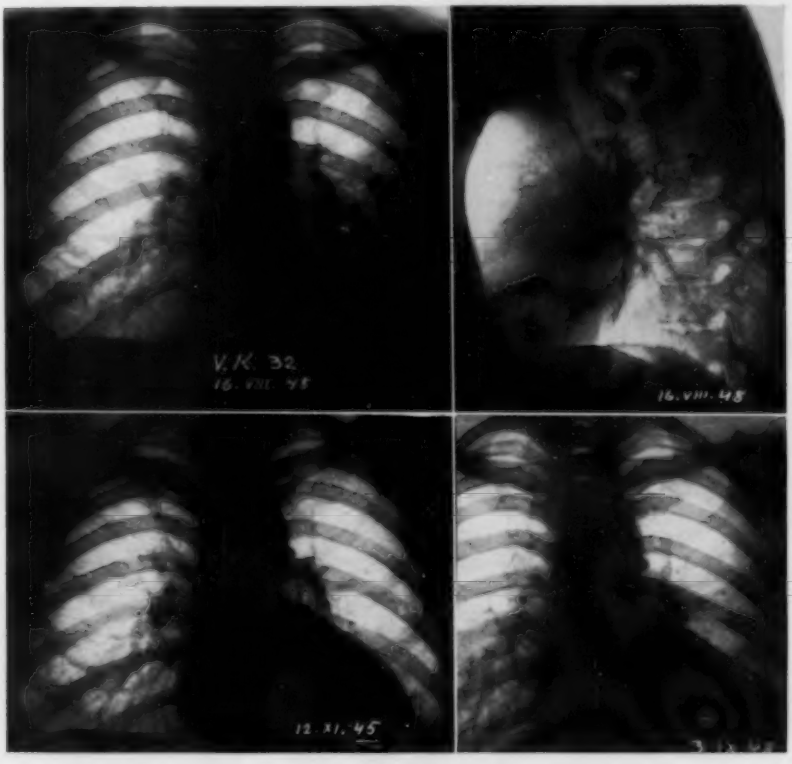
If each of the three tuberculosis groups of the table is subdivided furthermore according to the degree of parenchymal lesions, we find within the first group—Acute



CASE 3

Pleurisy—524 cases without any parenchymal processes whatsoever or only quite minimal ones, and 387 cases with obvious parenchymal lesions, known prior to the onset of pleurisy or developing, respectively discovered, in the course of the next two years. In 95 of the 524 cases without, or with minimal pulmonary processes signs of bronchostenosis were present, and in 429 no such symptoms had been demonstrated. The incidence rates relating to these stenosis-negative cases are, for AS 40.8 per cent and for ASta 40.6 per cent, the corresponding rates for the stenosis-positive cases being 64.2 per cent and 50.6 per cent respectively. As to the 387 pleurisy cases with obvious parenchymal processes prior to or following upon the pleurisy, the corresponding figures for the 238 cases without symptoms of stenosis are, AS 40.8 per cent and ASta 41.4 per cent, and for the 149 stenosis-positive cases, 61.1 per cent and 48.8 per cent respectively.

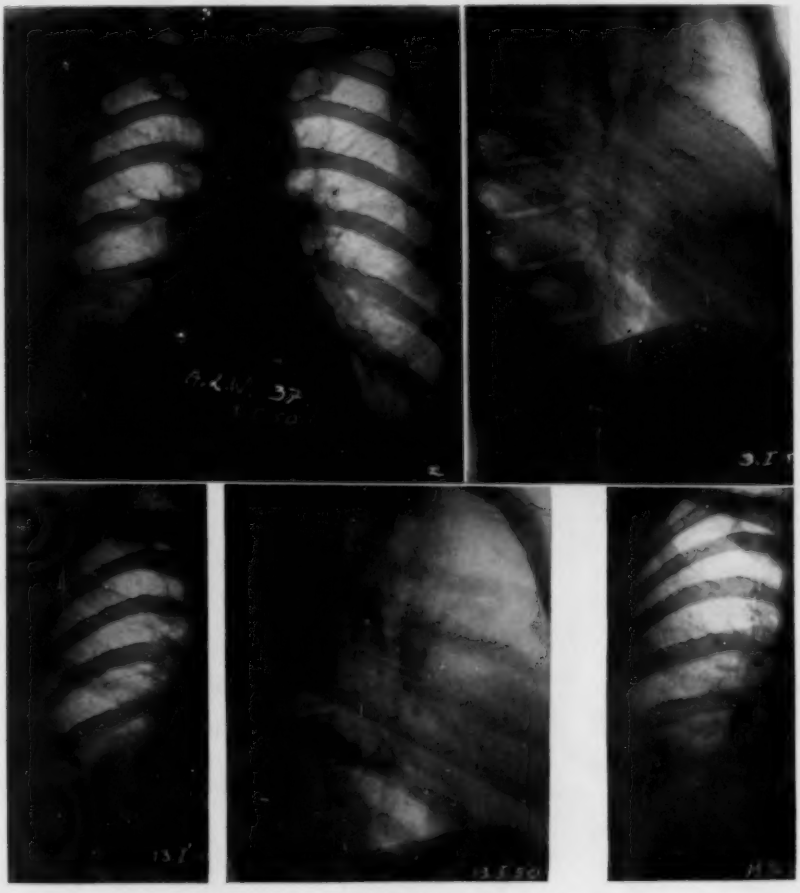
Similar conditions apply to the second group, the cases of pulmonary tuberculosis proper, where 744 of the patients had only minimal parenchymal lesions and 3,328 more pronounced processes (established or suspected cavity formation in more than one-half). Among these with minimal lesions 644 cases were negative as regards stenosis (with AS 37.3 per cent and ASta 30.4 per cent) and 98 positive (AS 62.2 per cent, ASta 54.6 per cent). Among the 3,328 cases with obvious parenchymal processes 2,145 were without demonstrated signs of stenosis (AS 40.4 per cent, ASta 32.8 per cent), and 1,183 were stenosis-positive (AS 65.3 per cent, ASta 53.7 per cent). Within the third tuberculosis group—Relatively Healed—335 patients at present and previously had but minimal processes, of whom 290 persons without symptoms of stenosis, with raised AS in 34.1 per cent and raised ASta in 24.9 per cent and 45 of the patients were stenosis-positive, with incidence rates of 57.8 per cent for AS and 40.0 per cent for ASta. Lastly, among the "healed" cases where evident pulmonary lesions were or had been present (more or less obvious cavity formation had been considered to exist in almost one-half of these instances) signs of stenosing processes had not



CASE 4

been noticed in 414 (AS 31.2 per cent, ASta 20.8 per cent) *versus* 208 cases with positive symptoms of this type and with the incidence rates 40.4 per cent for AS elevation and 35.7 per cent for ASta elevation.

Hence we find that the incidence of titre rises within all three tuberculosis groups is much the same in cases with pronounced parenchymal processes and in those where the lungs had been affected only to a very slight degree or not at all (in the pleurisy cases), and even with this subdivision the difference between the incidence rates for cases with or without signs of stenosis is apparent, with equal force, practically everywhere (10 of the relevant 12 difference figures are statistically supported). The fairly consonant results of the titre investigations in cases with slight and pronounced pulmonary lesions is but one of the many arguments that can be raised against the interpretation of the titre elevation as manifestation of some kind of "secondary infection" in relation to the tuber-



CASE 5

culous process (cp. also, e.g., the results of follow-up with both these titres recorded in 1945).[11]

In this connection also the incidence of bronchostenosis symptoms within the three tuberculosis groups may be mentioned. Among the Acute Pleurisy cases such symptoms have been recorded in 18.1 per cent of the cases without or with minimal pulmonary lesions, and in 38.5 per cent of the cases with parenchymal processes. In the Pulmonary Tuberculosis group the cases with but minimal lesions had shown signs of bronchostenosis in 13.2 per cent, as against 35.5 per cent of the more advanced cases, and among the "Healed" cases the corresponding incidence figures are 13.4 per cent and 33.4 per cent, respectively.

These figures cannot claim to give the true incidence of bronchostenotic phenomena but the relative values in consideration of the different groupings, and of parenchymal lesions seem to deserve some attention.

Cases of "Non-specific" Bronchostenosis

The connection of non-specific infections with bronchostenosis phenomena in tuberculosis cases has previously been pointed out. Also concerning the non-tuberculous pulmonary conditions the incidence figures in Table I indicate that similar non-specific infections may be apparent in association with processes encroaching upon the bronchial lumen.

If radiograms and bronchoscopic findings are examined not merely from the standpoint of practical diagnosis, i.e., usually in respect of the question, tumour of tuberculosis, fairly frequently cases are found where either possibility can sooner or later be ruled out, but where bronchoscopy or bronchography has disclosed symptoms of bronchial constriction persisting or more transient in nature. Some few instances of this type (included in the clinical group "Various acute non-tuberc. pulmon. conditions" of Table I) may be briefly quoted. Now and then papers on the so-called middle-lobe-syndrome have appeared, and no doubt that phenomena such as demonstrated in this series are most clearly observed in cases of this localization, but the same type of process may be met with in all parts of the lungs, and principally the same pathogenesis can be assumed.

In the following cases one to six (all women) shortly and simply "bronchopneumonia" might be stated as the diagnosis, and in some of them the onset and the general clinical picture was conforming to this type of disorder. In cases two, three and four at first a bronchial carcinoma was actually suspected, and even in the other three cases such an aetiology might have been possible. In all instances there was more or less coughing, and in some cases slight subjective symptoms of the kind that are often noted in association with pronounced bronchostenosis. The amounts of sputum were small or nil in cases one to four, in cases five and six fairly large quantities of sputum were reported, but only for a few days. All the cases were moderately sensitive to tuberculin, but repeated examinations of sputa for tubercle bacilli were negative, and also culture tests of sputum and gastric lavage. In none of these cases development of tuberculosis (or other serious trouble) ensued.

Among individual details and the results of bronchoscopy only the following should be mentioned:

Case 1: M. L. aged 38, is a fairly typical instance of a temporary "middle lobe syndrome." Marked regression in the x-ray film from Feb. 4, on March 1 practically full regression. Bronchoscopy on Feb. 8 still showed some general swelling of the bronchial mucosa, chiefly on the right side and especially of the middle lobe bronchus (probably some earlier chronic constrictions together with acute swelling).

Case 2: E. W. aged 47. A very marked atelectasis of the right upper lobe, suggestive of tumour, with rapid spontaneous regression. Bronchoscopically (Feb. 7) only some swelling and mucous discharge was to be observed.

Case 3: E. O. A. aged 48. In the history the development of rightsided central processes could be traced for one or two months. In the x-ray film June 27 some pleural effusion was suspected, but punctures were negative. Bronchoscopy (July 27) disclosed a very pronounced swelling of non-characteristic type with almost complete constriction of the right lower lobe bronchus. Biopsy no typical findings. X-ray films after

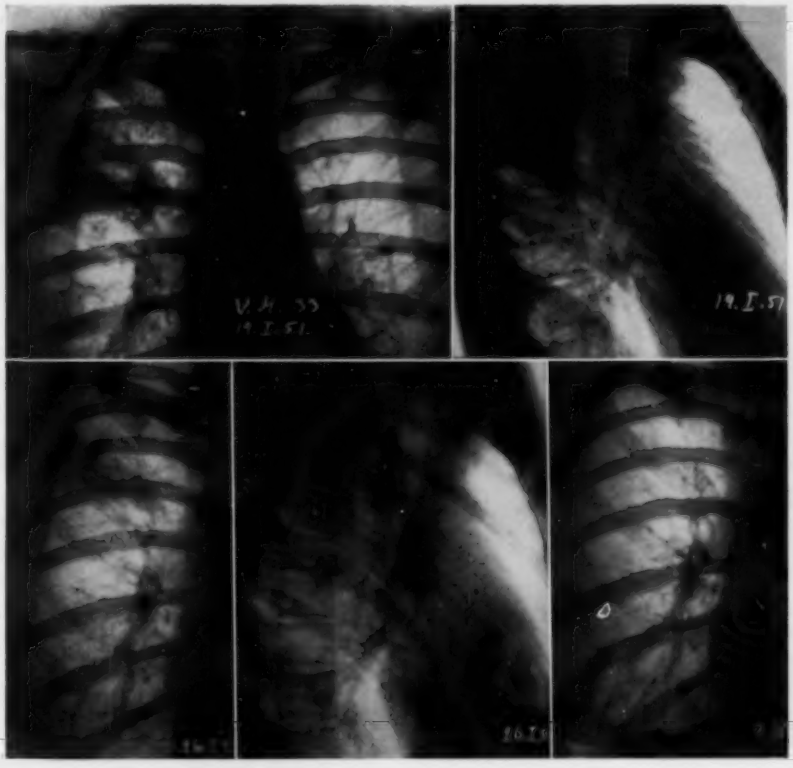
some weeks showed regression, and on Aug. 13 only some hilar node swelling was visible. Repeated bronchoscopic examinations showed regression, but even on Oct. 20 some stenosis of the lower lobe bronchus could be seen.

Case 4: V. K. aged 32. Atelectasis of the lower segment of the left upper lobe. Suspicion of tumour, bronchography and biopsy findings much the same as in Case 3. Rapid spontaneous regression. On Sept. 3, 1948 the same x-ray picture as three years earlier (1945), with strongly marked calcification of the hilar nodes.

Case 5: A. L. W. aged 37. Periodical cough and fever since October, at the end of December 1949 suddenly increased sputum, suggesting pulmonary abscess, and in the x-ray film of Jan. 3 (and even on Jan. 13) a cavity in the posterior segment of the right lower lobe was visible. Bronchoscopy (Jan. 24) showed a marked swelling of the mucosa on the right side, especially in the lower lobe bronchus, with constriction. On Feb. 17 the acute swelling had practically subsided, but some stenosis of the bronchus was still observed. The clinical symptoms had now fully disappeared.

Case 6: V. H. aged 33. Much the same history and findings as in Case 5, but the abscess was situated in the right upper lobe. Bronchoscopically (on March 2), besides swelling and constriction of the right upper lobe bronchus a tracheobronchial indentation of lymph node type was observed. After a few days of penicillin treatment all symptoms were gone, but another bronchoscopy one month later showed a marked cicatricial stenosis of the anterior branch of the upper lobe bronchus.

Phenomena of a more or less pronounced atelectasis in the x-ray film were observed in all the cases and at least in five they were evidently secondary to a constriction in the bronchial area involved. In some instances it could be stated that a certain degree of bronchostenosis had



CASE 6

preceded the acute onset of the infection. In all cases of this kind, however, it appears justified to assume that there has been some previous abnormality in respect of the bronchial wall, and that an acute inflammatory process had provoked the local narrowing. The anatomical bases of such a preformation is to be sought, above all, in the lymphatic system, and as far as I can see, sequelae of previous, healed tuberculous lesions should here be considered. Certainly such a derangement need not be so pronounced as to be grossly visible on an ordinary *post-mortem* inspection, and unfortunately, methods of more detailed study of minute alterations within the lymphatic system seem so far to be lacking.

Hence, the cases quoted can as yet chiefly serve to focus attention on comparatively typical processes, clinically often involving difficulties of differential diagnosis. The present paper aims in the first place at demonstrating that non-specific infections, to which ordinarily no attention is paid, may give rise to important complications in cases of active pulmonary tuberculosis but sometimes even in patients which must be recorded as non-tuberculous.

SUMMARY

A material of about 6,000 cases of pulmonary tuberculosis (including acute pleurisy) and 691 cases of non-tuberculous pulmonary diseases was investigated in respect to serum titres (the antistreptolysin titre regarding beta-haemolytic streptococci and the antistaphylolysin titre for yellow staphylococci). Elevation of these titres occurred to a great extent among the tuberculosis cases (least among those probably healed). In the group of non-tuberculous disease of the lung the asthma and carcinoma cases show comparatively low incidence of titre rises. The titre elevation should be regarded as indicating an active infection by the respective bacteria, but beyond this even other, non-specific pathogens are certainly active to the same or a still greater extent. Particularly as regards the tuberculosis cases such multiple or supervening infections on the whole should not be deemed "secondary infections." As a rule the incidence of titre elevations is highest in recent cases without marked pulmonary processes, and on the whole titre rises are nearly equally common whether the pulmonary lesions be minimal or very marked.

Cases with signs of bronchostenosis both in tuberculosis and in the groups of non-tuberculous pulmonary diseases exhibit roughly fifty per cent higher incidence rates or raised antistreptolysin titres, and a similar, though somewhat lower difference is noted also as regards the antistaphylolysin titre when the stenosis cases are compared to such instances where no symptom of bronchial obstruction had been recorded. The results of *post-mortem* bacteriological studies, *inter alia*, support the opinion that the non-specific infections are lodging specially in the lymph nodes of the respiratory system.

The cause of perforation processes or other types of encroachment of the process from the lymph nodes on to the bronchi, which subsequently may give rise to stenosing processes, is above all a clash within the node between a tuberculous process and one or several non-specific infections.

Non-specific infections may frequently, not least in cases of primary tuberculosis, concur with or be older than the tuberculosis process.

Chronic and acute non-specific infections may exert influence also in other ways, and such infections should be regarded as chief pathogenetic factors altogether in tuberculosis cases, and hence also as of considerable prognostical importance.

As examples of acute pulmonary conditions, similar in type, where active tuberculosis is certainly absent, are adduced six typical cases including one of the so-called middle-lobe syndrome.

RESUMEN

Un material de alrededor de 6,000 casos de tuberculosis pulmonar (incluyendo pleuresía aguda) y 691 casos de enfermedades pulmonares no tuberculosas, fué investigada respecto a valores en el suero (concentracién de antiestreptolisina en relación con el estreptococco beta-hemolítico y la concentración de antiestafilolisina para los estafilococos aureo). Hubo elevación de estos valores en gran número entre los casos de tuberculosis (menos entre los probablemente curados). En el grupo de enfermedades no tuberculosas del pulmón, los casos de asma y carcinoma presentan una frecuencia relativamente baja de elevación de los valores. La elevación de los valores rebe ser considerada como indicadora de una infección activa de las bacterias respectivas, pero además de estos, otros agentes patógenos no específicos están con certeza activos, en el mismo o en mayor grado. Particularmente en lo que se refiere a los casos de tuberculosis, esas infecciones múltiples o superpuestas, en conjunto no deben ser consideradas como "infecciones secundarias." Como regla la frecuencia de las elevaciones de los valores es la más alta en los casos recientes sin afecciones pulmonares marcados y en total las elevaciones de lo valores son casi igualmente comunes, ya sea que las lesiones pulmonares sean mínimas o acentuadas.

Los casos con signos de estenosis bronquial, tanto en tuberculosis como en los grupos de enfermedades pulmonares no tuberculosas, presentan un promedio de frecuencia de elevación de los valores de antiestreptolisina, de cerca del cincuente por ciento; y se nota también una diferencia similar; aún cuando algo menor en lo que respecta a los valores de antiestafilolisina cuando se comparan los casos de estenosis con las ocasiones en que no se anotaron signos de obstrucción bronquial. Los resultados de los estudios post-mortem bacteriológicos, en conjunto, soportan la opinión de que las infecciones no específicas se localizan en los ganglios linfáticos del aparato respiratorio.

La causa de los procesos de perforación u otros tipos de invasión del proceso de los ganglios linfáticos en los bronquios, que subsecuentemente puede dar lugar a procesos estenosantes, es sobre todo debido a una colisión dentro del ganglio entre el proceso tuberculoso y una o varias infecciones no específicas. Las infecciones no específicas pueden frecuentemente, por lo menos en casos de primo-infección tuberculosa, concurrir o ser anteriores al proceso tuberculoso.

Las infecciones no específicas tanto crónicas como agudas pueden también ejercer influencia de otras maneras, y tales infecciones deben ser consideradas como factores patogenéticos principales en conjunto en casos de tuberculosis y por lo tanto también como de considerable importancia pronóstica.

Como ejemplos de padecimientos agudos pulmonares, similares en su tipo, en los cuales hay ausencia positiva de tuberculosis activa, se aducen seis casos típicos, incluyendo uno del llamado síndrome mediolobar.

RESUME

L'auteur a étudié 6.000 cas de tuberculose pulmonaire (comprenant la pleurésie aiguë) et 691 cas de maladies pulmonaires non tuberculeuses, en ce qui concerne le dosage des anticorps plasmatiques antimicrobiens (les antistreptolysines pour les streptocoques béta-hémolytiques et les antistaphylolysines pour les straphylocoques dorés). L'élévation de ces anticorps fut constatée dans un grand nombre de cas parmi les tuberculeux (moins parmi ceux vraisemblablement guéris). Dans le groupe des affections non tuberculeuses du poumon, les cas d'asthme et de carcinome montrent une fréquence relativement faible de l'élévation des immunisines. L'élévation des anticorps devrait être considérée comme indiquant une infection active par les germes respectifs, mais au-delà de cette indication, on pourrait admettre également que les microbes pathogènes non spécifiques sont certainement actifs dans une proportion semblable ou même plus grande. Particulièrement lorsqu'il s'agit de cas de tuberculose, de telles infections multiples ou surajoutées ne devraient pas être étiquetées dans l'ensemble "infections secondaires." En règle la fréquence de l'élévation des anticorps est plus grande dans les cas récents, sans processus pulmonaires nets, et dans l'ensemble, les élévations des anticorps sont presque également banales, qu'il s'agisse de lésions pulmonaires minimes ou accentuées.

Les porteurs de sténose bronchique (à la fois dans la tuberculose et dans les groupes d'infections non tuberculeuses) montrent grossièrement une augmentation de plus de 50% des antistreptolysines, et un taux semblable, quoique l'on puisse noter une différence un peu plus faible, en ce qui concerne les antistaphylolysines, lorsqu'on établit une comparaison avec les cas de sténose où aucun symptôme d'obstruction n'a été enregistré.

Le résultat des études bactériologiques post-mortem, entre autres, donne à penser que les infections non spécifiques ont leur siège dans les ganglions lymphatiques du système respiratoire.

La cause des processus de perforation ou d'autres sortes d'agressions provenant des ganglions dans les bronches, qui par conséquent peuvent donner lieu à un processus de sténose, est surtout la *collision* à l'intérieur d'un nodule entre un processus tuberculeux et une ou plusieurs infections non spécifiques. Les infections non spécifiques peuvent fréquemment, au moins dans les cas de tuberculose primaire, survenir pendant ou avant le processus tuberculeux.

Les infections non spécifiques chroniques et aiguês peuvent aussi exercer

une influence dans d'autres domaines et de telles infections doivent être considérées comme des facteurs pathogéniques importants dans les cas de tuberculose et delà aussi leur importance considérable du point de vue du pronostic.

Les auteurs ajoutent six cas typiques comprenant un cas de soi-disant "syndrome du lobe moyen" comme exemple d'états pulmonaires aigue, de type semblable, où une tuberculose active est certainement exclue.

ZUSAMMENFASSUNG

Ungefähr 6000 Fälle von Lungentuberkulose, einschliesslich akuter Pleuritis, und 691 Fälle nicht tuberkulöser Lungenerkrankungen wurden hinsichtlich ihres Serum-Titer untersucht (der Antistreptolysin-Titer bezüglich der beta-haemolytischen Streptokokken und der Antistaphylosin-Titer für gelbe Staphylokokken). Ein grosser Teil der Tuberkulose-Fälle zeigt eine Erhöhung dieser Titer; diese Erhöhung zeigte sich am wenigsten bei den anscheinend geheilten Fällen. In der Gruppe der nicht tuberkulösen Lungenerkrankungen, beim Asthma und beim Karzinom konnte relativ selten eine Titer-Erhöhung gefunden werden. Die Titer-Erhöhung ist als ein Zeichen der aktiven Infektion durch die entsprechenden Bakterien zu werten; darüber hinaus sind jedoch auch andere unspezifische pathogene Keime in gleichem oder höherem Masse wirksam. Im ganzen sollten besonders hinsichtlich der Tuberkulose solche Misch- oder zusätzlichen Infektionen nicht für "Sekundär-Infektionen" gehalten werden. In der Regel ist die Titer-Erhöhung am grössten bei frischen Fällen ohne deutlichen Lungen-Prozess, und im ganzen gesehen sind die Titer-Erhöhungen etwa gleich häufig geringfügigen und deutlichen Lungenveränderungen.

Fälle mit Anzeichen der Bronchostenose weisen sowohl bei Tuberkulose als auch bei nicht tuberkulösen Lungenerkrankungen ca. 50% häufiger einen erhöhten Antistreptolysin-Titer auf. Die Erhöhung des Antistreptolysin-Titers findet sich etwas seltener bei Fällen mit Stenose im Vergleich zu Fällen ohne Symptome von Bronchial-Verengung. Die Resultate der postmortalen bakteriologischen Untersuchungen bestätigen unter anderen die Ansicht, dass die unspezifischen Infektionen sich besonders in den Lymphknoten des Respirationstraktes befinden.

Die Ursache zur Perforation oder anderen Arten des Eindringens des Prozesses von den Lymphknoten in die Bronchien, durch die späterhin der stenosierende Prozess hervorgerufen wird, ist vor allem das Zusammentreffen zwischen tuberkulösem Prozess und einer oder mehrerer unspezifischer Infektionen im Lymphknoten. Unspezifische Infektionen können häufig — besonders in Fällen von Primär-Tuberkulose — mit dem tuberkulösen Prozess zusammen auftreten oder älter als derselbe sein.

Chronische und akute unspezifische Infektionen können auch in anderer Weise wirken; und solche Infektionen sollten in ihrer Gesamtheit als wesentliche pathogenetische Faktoren bei der Tuberkulose angesehen und ihnen daher auch beträchtliche prognostische Bedeutung beigemessen werden.

Sechs typische Fälle, einschliesslich eines Falles des sogenannten Mittellappen-Syndroms werden als Beispiele ähnlicher Lungenerkrankungen ohne Vorhandensein von Tuberkulose angeführt.

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Pulmonary Resection in Pregnancy

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After nearly a quarter of a century of experience with planned, anatomical, pulmonary resection, the association of this type of surgery with pregnancy is still an extremely rare event. Lately the literature has begun to devote some space to descriptions of such occurrences. However, when it is realized that, of the first eight successful pneumonectomies, six were performed on women in, or younger than, the child-bearing years,[1] it is remarkable that more reports of pregnancy, at least subsequent to major pulmonary resection, have not appeared.

We have been able to collect only 62 reported cases of pulmonary resection accomplished prior to or during pregnancy, with some semblance of follow-up as far as subsequent course of the pregnancy is concerned. In addition to these, Pisani has made reference to 12 such cases observed in the Veteran's Administration hospitals without giving description of the fate of the fetus or the type of surgery.[3]

An analysis of the 62 cases is presented in Tables I and II. Forty-one (66.1 per cent) of the resections were done for pulmonary tuberculosis.[1, 2-7, 13] Fifteen (24.2 per cent) were for bronchiectasis[1, 8] and the remaining six (10.7 per cent) for carcinoma,[1, 9] hemangioma,[10] cystic disease,[11] and echinococcosis.[12]

Forty-seven (75.8 per cent) of the resections were accomplished prior to pregnancy. Only 15 cases (24.2 per cent) of pulmonary resection during the course of pregnancy were found.[1-4, 6, 7, 12] Of these latter cases 13 (86.6 per cent) were lobectomies or bilobectomies and only two (13.4 per cent) were pneumonectomies;[3, 4] 10 (66.7 per cent) were performed for tuberculosis and five (33.3 per cent) for miscellaneous causes, three bronchiectatics,[1] an adenoma[1] and an echinococcus cyst.[12] One stillbirth occurred, in association with the sole maternal death, a fetal and maternal mortality of 6.7 per cent. In one case caesarean section[1] was elected. The remainder were delivered from below.

Nowhere have we found reference to pneumonectomy in the course of gestation accompanied by a "space-filling" procedure, thoracoplasty or plombage. We wish to present a third case of pneumonectomy during pregnancy. As far as we have been able to learn, this is the first such procedure done for non-tuberculous disease and the only case accompanied

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The opinions expressed are those of the authors and do not necessarily reflect the opinions or policies of the Air Force.

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1 (Case 1): Admission x-ray showing left lower lobar atelectasis.—*Figure 2 (Case 1):* Bronchogram demonstrating total bronchiectasis of left lung. A small area of the apical sub-segment appeared to be relatively normal; however, even this was found to be involved after removal of the lung.—*Figure 3 (Case 2):* Postpartum film. The regenerated ribs are evident beneath the Lucite® spheres.

TABLE I
PULMONARY RESECTION AND PREGNANCY

Analysis of Maternal Factors in 62 Reported Cases

	Indication			Mortality			
	Tuberculosis	Bronchiectasis	Other	Tuberculosis	Bronchiectasis	Other	Per Cent
1. RESECTION DURING PREGNANCY							
Pneumonectomy	2	0	0	0	0	0	0
Lobectomy	8	3	2	0	1*	0	7.6
Total	10	3	2	0	1	0	6.7
2. RESECTION PRIOR TO PREGNANCY							
Pneumonectomy	23	3	3	0	0	0	0
Lobectomy	8	9	1	0	0	0	0
Total	31	12	4	0	1	0	0
Grand Total	41	15	6	0	1	0	1.6

*Concurrent death of child.

TABLE II
PULMONARY RESECTION IN PREGNANCY

Analysis of Fetal Fate in Gestations

	Living Child			Abortion						
				Induced			Spontaneous			
	Tbc	B'ectasis	Other	Tbc	B'ectasis	Other	Tbc	B'ectasis	Other	Gross Mortality Per Cent
1. RESECTION DURING PREGNANCY										
Pneumonectomy	2	0	0	0	0	0	0	0	0	0
Lobectomy	8	2	2	0	0	0	0	1*	0	7.7
Total	10	2	2	0	0	0	0	1	0	6.7
2. RESECTION PRIOR TO PREGNANCY										
Pneumonectomy	26	3	4	4	0	0	2	1	0	17.5
Lobectomy	3	10	1	0	2	0	0	0	0	12.5
Total	29	13	5	4	2	0	2	1	0	16.1
Grand Total	39	15	7	4	2	0	2	2	0	14.1

by a space-filling plombage. Additionally, we wish to present a fourth case of lobectomy for bronchiectasis during pregnancy.

Case 1: Mrs. J. N. (Reg. No. 99785) A 17 year old white woman, Gravida II, Para I, Abortio O, LMP December 25, 1953, was referred to the 3810th USAF Hospital on February 10, 1954, because of an abnormality noted in her chest roentgenogram (Figure 1) and a history of recurrent bouts of severe pneumonitis, chronic cough, foul sputum, blood streaking, and occasional episodes of frank hemoptysis.

An elder sister had undergone left pneumonectomy for a total bronchiectasis in 1947 at 18 years of age. Her mother had apparently died of some chronic, non-tuberculous, suppurative, pulmonary disease.

The sister did well immediately following her surgery but lately has noted increasing dyspnea associated with palpitation and diminished exercise tolerance. A chest plate reveals a mediastinal shift to the left, with distension of the right lung and herniation of this lung into the left hemithorax.

At bronchoscopy our patient was seen to have a severe, ulcerative bronchitis on the left and bronchography (Figure 2) revealed total bronchiectasis on this side. The bronchitis was practically healed after a week of treatment with Alevaire® with two million units of penicillin and two grams of streptomycin in each five hundred milliliters administered as an aerosol for 30 minutes six times a day.

Sputum cultures done elsewhere were negative for tubercle bacilli, first and second strengths PPD were negative. Physical examination revealed consolidation of the left lower lobe. Pelvic examination showed findings consistent with a six week gestation. Chorionic gonadotropins were present in her urine.

Diagnoses of total left bronchiectasis and chronic abscess of the left lower lobe were made. She was given 25 milligrams of progesterone three times daily, and, after three days, left pneumonectomy was performed on March 2, 1954, under endotracheal anesthesia with Pentothal®, nitrous oxide and oxygen, supplemented by Anectine®. Postoperatively her course was benign. She was continued on progesterone, and, on March 23, 1954, under the same type anesthesia, a subcostal, extraperiosteal, Lucite® plombage was done to fill the pneumonectomy space. Again she made an uncomplicated recovery. She was maintained on progesterone 10 days post plombage and was discharged on April 3, 1954, two weeks following the final procedure. Diagnoses of total left bronchiectasis and chronic lung abscess were confirmed by gross and microscopic examination. S. aureus, H. influenzae, and N. perflava were cultured from the abscess cavity.

On September 29, 1954 (EDC October 2, 1954), after an uneventful, nine hour, slow labor, she was delivered of a 6 lb. 3½ oz., normal girl by low forceps under a saddle block. At no time did she show any sign of respiratory distress nor did the child at any time show signs of anoxia.

She was discharged on October 4, 1954. She is aware of sensations of the Lucite® spheres rubbing together at times, but this is apparently not distressing, and is not to be compared to the annoyance of the ronchus resulting from a small bronchial mucus plug. With the exception of this and moderate exertional dyspnea she is now asymptomatic. Postpartum chest x-ray films are shown (Figure 3).

Case 2: Mrs. L. S. (Reg. No. 103440) At age nine this 22 year old white woman was found to have right lower lobe bronchiectasis. Surgery was advised but not undertaken at the time. She entered the 3810th USAF Hospital complaining of chronic cough, wheezing, night sweats, recurrent respiratory infections and right chest pain. Para O, Gravida III, Abortio II (both in first trimester), LMP July 19, 1954.

Cultures of her sputum were negative for tubercle bacilli. First strength was negative, but second strength was positive. Bronchograms showed bronchiectasis of the right basal segments, the left basal segments, the lingula, and possibly the anterior segment of the left upper lobe (Figure 4). Bronchoscopy was negative. Pelvic examination revealed signs consistent with an eight week pregnancy.

She was placed on progesterone, 25 milligrams T.I.D., and, after a week of aerosol with Alevaire®, penicillin and streptomycin, on September 28, 1954, right basal segmental resection was performed under endotracheal anesthesia with Pentothal®, nitrous oxide, and oxygen, supplemented by Anectine®. Postoperatively she did well with the exception of some difficulty in expanding the remaining lung to completely fill the

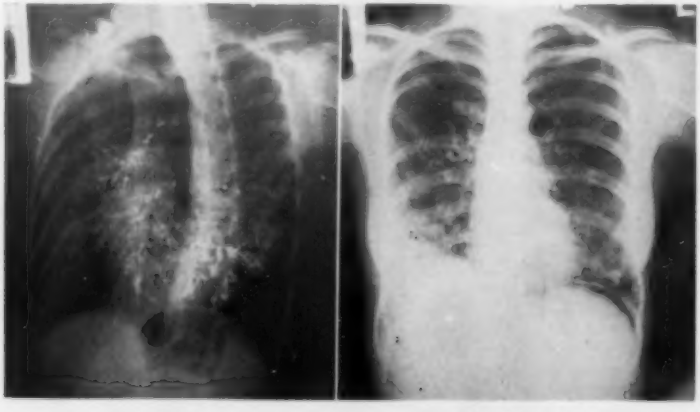

FIGURE 4 FIGURE 5

Figure 4 (Case 2): Preoperative bronchogram demonstrating widespread bilateral bronchiectasis.—*Figure 5 (Case 2):* Discharge film showing complete re-expansion of the right lung. A small amount of pneumoperitoneum remains. The right costophrenic angle is obscured somewhat by a post traumatic pleuritis.

pleural space at the right base. On the fourth postoperative day pneumoperitoneum was induced to assist in obliterating the space. Gentle suction was applied to the thoracostomy drains by a Gomco Thermotic Pump® and on the 11th postoperative day the space was obliterated and the tubes were removed. She was discharged on the 15th postoperative day (Figure 5). Progesterone was gradually discontinued.

When last seen she was in the sixth month of pregnancy, with no apparent complication, the furthest she had ever gone. Her cough was markedly diminished and she had had no episodes of pneumonitis and no significant chest pain.

We had planned to evaluate her further after delivery and probably to resect the diseased portions of her left lung. Unfortunately, her husband was transferred to another area and she will probably be lost to our follow-up.

Discussion

The ability of the pregnant woman to withstand rather severe degrees of ventilatory insufficiency, caused by absence of or compression of pulmonary parenchyma, has been well demonstrated by Gaensler[13] and others. Indeed, it might well have been inferred from the clinical histories of women, from the case of concomitant pregnancy and therapeutic pneumothorax described by Forlanini in 1906 to the present time, who had undergone collapse therapy for tuberculosis and who subsequently or simultaneously became pregnant. Apparently, too, by the same evidence, the fetus is not adversely affected. Among the 62 women described in the first portion of this paper and the two cases reported herein there were 73 reported pregnancies and only four spontaneous abortions, an incidence of 5.5 per cent, which compares favorably with the general population.

Among the 15 women reported submitted to resection during pregnancy and our two cases one spontaneous abortion is described, a fetal mortality of 5.9 per cent. In this case the mother developed, in the preantibiotic era, a postoperative broncho-pleural fistula and empyema. Her infection failed to respond to sulfapyridine. She ran a septic course with marked hyperpyrexia and aborted on her 14th and died on her 22nd postoperative day. Certainly it is possible, with the further developments in chest surgery, and with modern antibiotics, today, she might not have aborted and she might not have died. The ability of the pregnant woman to maintain pregnancy and withstand surgery has been well documented.

Judging from our own limited experience and from the equally limited reports in the literature, pulmonary resection in pregnancy is not fraught with danger to the mother, any more than to her non-pregnant sister. Neither is it fraught with danger to the fetus.

It has been pointed out that amenorrhea has been relieved and pregnancy has occurred in women previously sterile following extirpation of bronchiectatic lung. Our patient, Mrs. L. S., is now apparently carrying her baby to term, or at least to a viable state, following removal of what may well have been, judging from her symptoms, the most grossly infected portion of her lungs. Twice before she has failed to do this. Any conclusions we may draw from this one case are, of course, pure speculation. On the other hand further experience may well support the implied premise.

The relationship between the spread of tuberculosis and the emptying of the uterus at parturition has long been recognized.[14] It was somewhat surprising to us, therefore, to find, after eight years of generally

increasing acceptance of resectional surgery for tuberculosis, the relative paucity of the literature dealing with such therapy in the face of pregnancy. Certainly the indication must arise more often than one would be led to believe from reported cases.

We do not feel that surgery should be lightly undertaken in any patient. However, if the indication for pulmonary resection is present and is sound, we feel pregnancy presents no contraindication. Certainly therapeutic abortion should never be undertaken lightly. Aside from fetal destruction there is even evidence it may encourage dissemination of tuberculosis.[14] In any case, we feel sure there is absolutely no indication for advising therapeutic abortion prior to or after pulmonary resectional surgery, based on surgical or respiratory considerations alone.

If the underlying disease is one which will brook delay in its treatment, and if it is not one the dissemination of which may be encouraged by parturition, there appears to be reason to delay intervention after the seventh month of pregnancy. Surgery at such time is felt to encourage onset of premature labor and the child may be forced to assume an unwarranted risk.[7]

SUMMARY

1. The authors have been able to collect from the literature only 62 reported cases of pulmonary resection in association with pregnancy. Forty-seven were accomplished prior to pregnancy, and only 15 cases of pulmonary resection during pregnancy.

2. In view of the fact that the indications for pulmonary resection frequently arise in women in or younger than child bearing years, the authors are surprised at the relatively paucity of the literature dealing with this subject.

3. It is felt that this probably represents unwarranted fear of possible dangers of surgery to the mother or the child or both, from this type of surgery during gestation. Two cases of successful pulmonary resection during gestation are reported in an attempt to dispel fear and to encourage the more frequent employment of such resectional surgery, particularly in lieu of fetal destruction.

4. Our cases consist of one pneumonectomy followed by plombage done for bronchiectasis, and one basal segmental resection for bronchiectasis followed by pneumoperitoneum to elevate the diaphragm.

RESUMEN

1. Los autores han podido reunir solamente 62 casos publicados en la literatura médica en los que se ha hecho resección pulmonar antes o durante el embarazo. Cuarenta y siete en los que se hizo resección antes del embarazo y sólo 15 de resección durante el embarazo.

2. En vista de que las indicaciones para la resección pulmonar se presentan frecuentemente en mujeres en la edad fértil o antes, los autores se sorprenden de la relativa escasa literatura al respecto.

3. Se cree se debe a un temor injustificado a los peligros de la cirugía para la madre, el niño o ambos, durante la gestación.

Se relatan dos casos de resección durante la gestación con el fin de des-

cartar el temor y alentar hacia el uso más frecuente de la cirugía de resección, especialmente en lugar de la destrucción del feto.

4. Nuestros casos consisten en un neumonectomía seguida de plombaje hecha por bronquiectasis y una resección basal segmentaria por bronquiectasia seguida de neumoperitoneo para elevar el diafragma.

RESUME

1. Les auteurs n'ont pu réunir d'après la littérature que 52 observations de grossesse avec résections pulmonaires. 47 avaient été pratiquées avant et quinze seulement l'ont été au cours de la grossesse.

2. Remarquant que les indications de la résection pulmonaire sont fréquemment posées chez les femmes à l'âge de la maternité ou avant cet âge, les auteurs sont étonnés de la relative pauvreté de la littérature à ce sujet.

3. Ils ont l'impression que c'est la conséquence d'une crainte non fondée des dangers possibles de l'intervention sur la mère et l'enfant ou sur les deux, quand elle est pratiquée pendant la grossesse. Ils rapportent deux cas de résection pulmonaire satisfaisante exécutée au cours de la grossesse, pour essayer de faire disparaitre toute crainte et pour encourager l'emploi plus fréquent d'une telle intervention, en particulier à la place de l'interruption de grossesse.

4. Les observations des auteurs comprennent une pneumonectomie suivie de plombage, faite pour bronchiectasie, et une résection segmentaire de la base pour une bronchiectasie, suivie d'un pneumopéritoine pour su rélever le diaphragme.

ZUSAMMENFASSUNG

1. Es war den Verfassern lediglich möglich, aus der Literatur 62 Berichte zu sammeln über Fälle von Lungenresektion in Verbindung mit Schwangerschaft. 47 wurden vor der Schwangerschaft vorgenommen und nur 15 Fälle von Lungenresektion während der Schwangerschaft.

2. Im Hinblick auf die Tatsache, dass die Indikationen zur Lungenresektion häufig gestellt werden bei Frauen im oder vor dem gebärfähigen Alter, sind die Verfasser überrascht von der relativ spärlichen diesen Gegenstand betreffenden Literatur.

3. Es wird die Auffassung vertreten, dass darin wahrscheinlich eine unberechtigte Furcht vor möglichen Gefahren der Operation für die Mutter oder für das Kind oder für beide zum Ausdruck kommt und zwar von dieser Operationsart während der Schwangerschaft. 2 Fälle von erfolgreicher Lungenresektion während der Schwangerschaft werden wiedergegeben als ein Versuch, die Furcht zu verstreuen und Mut zu machen zu einer häufigeren Anwendung solcher Eingriffe mit Resektionen besonders anstelle der Tötung fetalen Lebens.

4. Unsere Fälle bestehen aus eine Pneumonektomie mit anschliessender Plombierung, die wegen Bronchiektasie ausgeführt wurde, und einer basalen Segmentresektion wegen Bronchiektasie mit anschliessendem Pneumoperitoneum zwecks Hochstellung des Zwerchfelles.

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Intracardiac Extension of a Bronchogenic Carcinoma*

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The heart and pericardium are by no means exempted[3] from metatases from bronchogenic carcinoma but considering the anatomic proximity of the heart to the lungs it is surprising that cardiac metastasis occurs but in 8 to 10 per cent of cases reported by various authors.[1, 2] Being a malignant tumor, pulmonary carcinoma frequently penetrates pulmonary veins and their tributaries (five instances are cited by Willis[3]). Rarely, it may extend into the heart. One such case was reported by Whiteley.[4]

We would like to present the following which is the first reported case of intraventricular extension of bronchogenic carcinoma in the literature.

J. W. (Hospital No. 40954), a 63 year old white man, bus driver, was admitted for the chief complaints of indigestion, chest pain, and cough. On physical examination, the right lung was found to be emphysematous. The heart was enlarged, the rhythm was irregular, and a grade II systolic murmur was heard over the aortic valve. Blood pressure was 95/60 mm. of Hg. X-ray film of the chest revealed old pulmonary tuberculosis with emphysema and a left hilar mass. He was discharged after 10 days with a diagnosis of inoperable carcinoma of the left lung.

He was readmitted a month later with severe dyspnea and bilateral axillary lymphadenopathy. Cardiac findings remained the same. He died five days later with symptoms of respiratory failure.

The past history revealed that he had been admitted at another hospital four years before death, complaining of chills, fever, and pain in the left lower chest. At that time, the lungs were found to be hyperresonant in both bases with asthmatic wheezes throughout both lungs. The heart was normal. X-ray film of the chest revealed a density in the left costo-phrenic angle interpreted as acute pleurisy with effusion and possible pneumonitis.‡ The right lung was emphysematous. *No tumor mass was seen.*

The pertinent necropsy findings were in the lungs and heart. In the left upper pulmonary lobe there was a pedunculated nodular firm tumor mass measuring 7.0 cm. in diameter. It was attached to the upper left descending bronchus by a firm narrow pedicle measuring 2.5 cm. in length and with an average diameter of 0.5 cm. The heart was enlarged and weighed 500 Gms. A firm, 14.0 cm. long tumor mass protruded from the median pulmonary vein into the left ventricle completely plugging the mitral opening (Fig. 1). The intracardiac mass was pear-shaped, with the proximal end measuring 4.0 cm. in average diameter and the distal portion 10.0 cm. in diameter. The mass was not adherent to the endocardium. Neither were there intrinsic lesions on the valves. Sections through the pulmonary and intracardiac tumors revealed irregularly lobulated, firm, mottled gray pink tissue. *No other gross metastases were seen.*

Microscopic examination disclosed a pleomorphocellular malignant neoplasm. At the site of origin in the bronchus the tumor had a typical

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oat-celled pattern with loose aggregates of small round to ovoid cells with scanty cytoplasm and fine reticulated stroma. There were areas where the cells were in small clumps and nests with peripheral palisading suggestive of a carcinoid type of bronchial adenoma. This histologic configuration was seen at the site of penetration of the tumor into the pulmonary vein (Fig. 2). With increasing distance from the site of origin, the tumor assumed a different architecture. The cells became polygonal and large and arranged in solid sheets and islands with definite cobble-stone pattern (Fig. 3). There was definite evidence of keratinization with well-formed

FIGURE 1: Opened left atrium and ventricle of heart with neoplasm. (Note the stem of tumor within the pulmonary vein). Scale: Reduced 20 per cent (see cm. ruler).

epithelial pearls. The tumor stroma in these areas was made up of dense collagenous fibers. The same microscopic picture was seen in the intracardiac mass (Fig. 4). The tumor as a whole was extensively necrotic. There was focal lymphocytic infiltration of the stroma. *The other organs were free of metastases.*

Discussion

Aside from its rarity, this case presents several interesting facets in its clinical and pathologic picture.

The history of chronic cough and asthma of long standing becomes quite interesting in the light of the findings of one of the authors[5] who studied cases of bronchogenic carcinoma admitted to the Ohio State University Hospital in the year 1952-1953. About two thirds of the patients studied gave a history of "asthma." While it is difficult to draw a cause-and-effect relationship between chronic cough, asthma, and bronchogenic carcinoma, the frequent association of these three conditions with the cough and asthma usually antedating the neoplasm should attract attention of all interested in the problem of lung cancer.

As emphasized in the clinical history, the findings of cardiac enlargement, arrhythmia, and aortic systolic murmur coincided with the discovery of the lung tumor. Four years before, the heart was essentially normal. It is difficult to state that the same findings would be present in all cases of intracardiac tumor in the left atrium or ventricle. But, the presence of a left hilar tumor mass, the sudden appearance of such cardiac abnormalities should alert the clinician to the possibility of intracardiac extension of a pulmonary neoplasm. Undoubtedly, electrocardiographic studies or cardiac catheterization would have provided valuable diagnostic clues. Unfortunately, the patient expired before requests for such studies could be filled.

The absence of distant metastases makes our case and the few other similar cases reported unique among patients who succumb to bronchogenic carcinoma. At first glance, it seems paradoxical for a malignant tumor to remain localized after it has penetrated the general circulation. One should consider, though, that intravenous and intracardiac extension of a bronchogenic tumor is still an integral part of the main tumor mass and is more cohesive since it carries with it its own tumor stroma. In contrast to this, a tumor embolus is as a rule only a nest or loose aggregate of tumor cells which has been detached from the main new growth. Another logical explanation for the absence of remote metastasis is the possibility that intracardiac extension is a lethal complication and that the patient dies before distant metastasis has developed.

To the pathologist, the pleomorphism of the neoplasm in our patient is striking. There was hesitation as to the proper classification of the tumor. The question came up whether this is an oat-celled type of bronchogenic carcinoma with extensive squamous metaplasia, whether this malignant tumor arises from a carcinoid type of bronchial adenoma, or whether it is a poorly differentiated squamous carcinoma of the bronchus. The

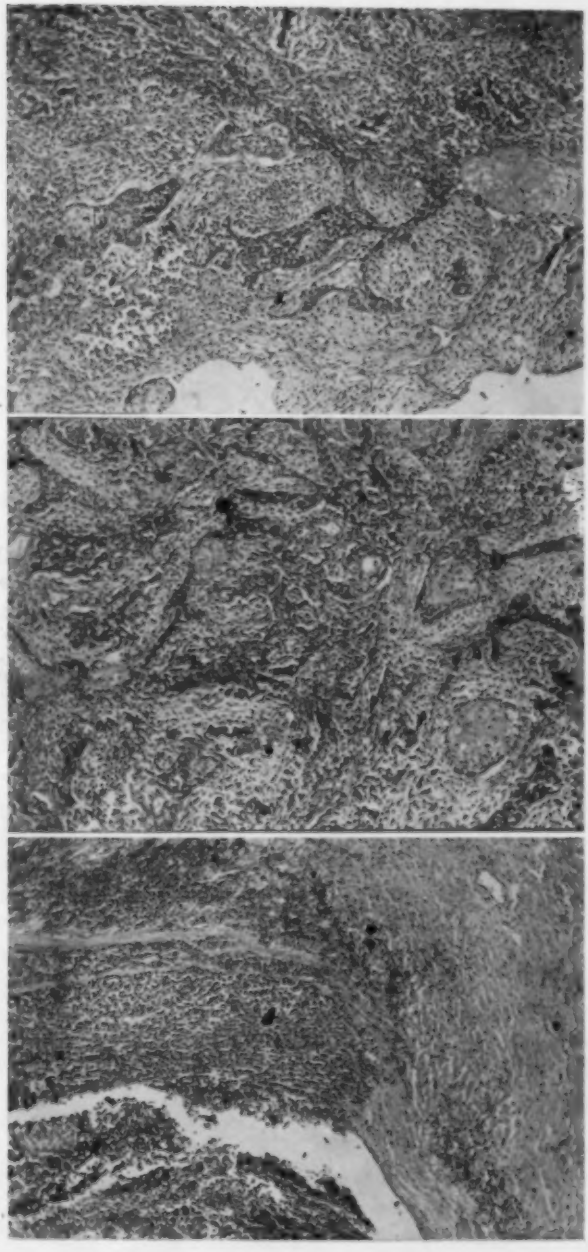

FIGURE 2

FIGURE 3

FIGURE 4

Figure 2: Penetration of neoplasm into pulmonary vein (X 110).—*Figure 3:* Architecture of primary pulmonary neoplasm—Oat-celled carcinoma with squamous metaplasia (X 150).—*Figure 4:* Architecture of neoplasm within the heart (identical with the sections from the main tumor mass in the lung), (X 150).

presence of all these histologic features in a tumor brings out the question whether our classification of bronchogenic carcinoma into definite cell types might be too arbitrary. Drawing a corollary with breast carcinoma, where sections taken at various levels through the same tumor mass as a rule give a varying histologic picture as far as cell type and stroma are concerned, probably serial sections through a bronchogenic carcinoma would likewise give a pleomorphic picture such as we see in our case. Aware of the totipotentialities of the alveolar and bronchiolar epithelium and to be in accord with the accepted modes of classification, we are inclined to call the new growth an oat-celled type of bronchogenic carcinoma with squamous metaplasia. Whether the tumor originally started as a bronchial adenoma of the carcinoid type poses another question.

Acknowledgment: The authors wish to thank Dr. O. J. Pollak, pathologist at Beebe Hospital for assistance in the preparation of this paper.

SUMMARY

A rare case of bronchogenic carcinoma with intracardiac extension by way of the pulmonary vein is reported. Various points of clinical and pathologic interest presented by the patient and his new growth are discussed.

RESUMEN

Se relata un caso raro de carcinoma bronquiogénico con propagación intracardiaca por la vía de la vena pulmonar. Se discuten varios puntos de interés clínico y patológico en este enfermo y en el tumor que presentó.

RESUME

L'auteur rapporte un cas rare de cancer bronchique avec extension à l'endocarde par la veine pulmonaire. Différents points d'intérêt clinique et anatomique présentés par le malade et l'extension nouvelle de sa maladie sont étudiés.

ZUSAMMENFASSUNG

Wiedergabe eines seltenen Falles von bronchogenem Carcinom mit intracardialer Ausbreitung auf dem Wege über die Lungenvenen. Die verschiedenen Punkte von klinischem und pathologischem Interesse, die der Kranke und sein neues Wachstum bietet, werden besprochen.

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The Effect of the Major Therapies on the Hospital Tuberculosis Mortality Rate*

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The tuberculosis mortality rate has been declining steadily for many years. In the last 50 years it has dropped approximately 90 per cent. There are at least four factors involved in this downward trend: 1. the natural law of selection of the fittest (the development of racial host resistance), 2. improved case finding so that more patients with better prognosis are included in the statistics, 3. improved standard of living, and 4. improved methods of therapy. The latter has accelerated the death decline in the last four years, a fact which is more readily demonstrated by correlating the trends in the major forms of therapy with the hospital mortality rate. It is the purpose of this report to show that the recent precipitous decline in deaths from tuberculosis at a large municipal general hospital is closely related to the use of prolonged combined antimicrobial regimens including streptomycin, para-aminosalicylic acid (PAS), and isoniazid.

The data presented cover the 11 years from 1943 to 1953 inclusive. During this period there have been some changes in the type of patient admitted to this institution's tuberculosis wards[1] but it is unlikely that these changes have greatly altered the over-all prognosis. Patients tend to be older, except for the Negro female. The favorable effect which this might have on the mortality rate is probably counterbalanced by the unfavorable effect of an increased proportion of Negro female patients. The percentage with advanced disease has not changed at all and the socioeconomic status has remained the same.

The major forms of therapy include rest, diet, temporary collapse procedures, antimicrobials and surgery. There have been no significant changes in the application of rest and diet. Surgical procedures have involved so small a number of patients, even in recent years, that their effect on the mortality rate can be neglected. Therefore temporary collapse procedures and antimicrobials have been correlated with the hospital mortality rate in Figure 1. Also plotted are curves for the average duration of hospitalization and the average daily census. In this graph the latter would have an effect only on the number of pneumothorax and pneumoperitoneum treatments given each year.

It can be seen that in 1951 the hospital mortality rate in terms of the percentage of all discharges for tuberculosis began to fall precipitously. Prior to this time deaths from tuberculosis ranged around 40 per cent but by 1952 the figures had fallen to about 18 per cent and levelled out. This change can *not* be correlated well with changes in the use of tempo-

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rary collapse. During the fall in mortality the use of pneumothorax rapidly fell to the vanishing point. The use of pneumoperitoneum began to rise in 1947 and rapidly reached a peak in 1951. At that point this procedure quickly lost favor and yet the mortality rate continued to fall markedly for another year before it levelled out. It is possible that the failure of the mortality rate to change between 1952 and 1953 is related

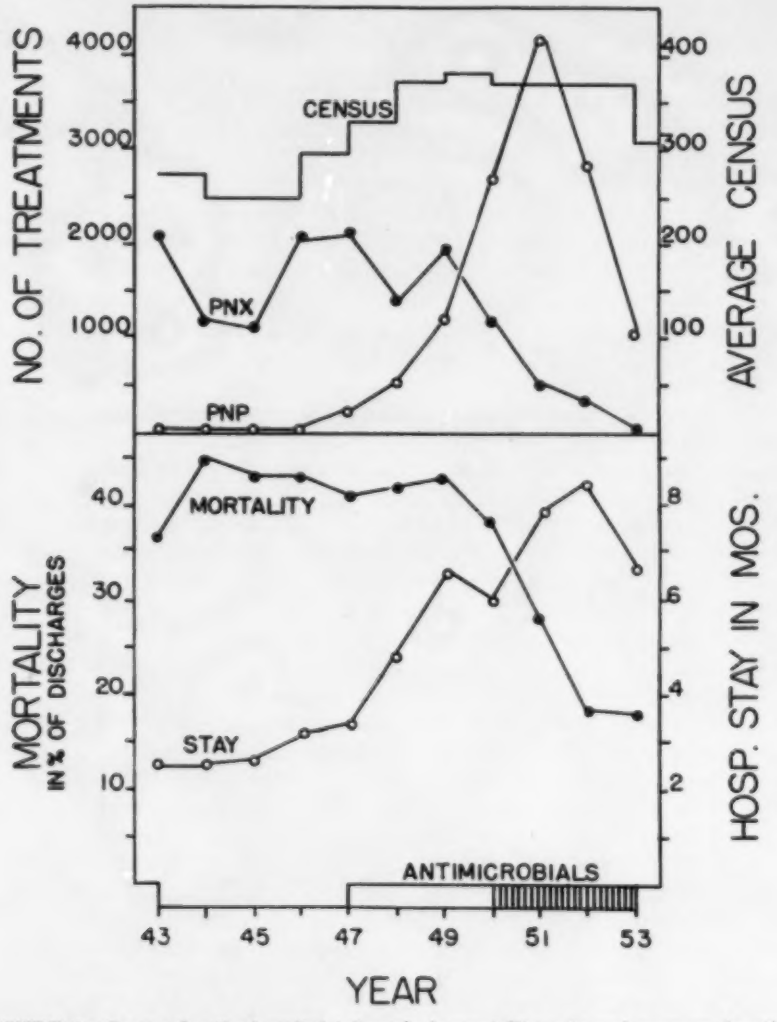

FIGURE 1: Curves for the hospital tuberculosis mortality rate and average duration of hospital stay correlated with the number of pneumothorax and pneumoperitoneum treatments, the average daily census, and the use of antimicrobial drugs by year from 1943 to 1953 inclusive. Significant use of antimicrobials began in 1947, prolonged combined regimens began in 1950 and isoniazid was introduced early in 1952. PNX means pneumothorax and PNP means pneumoperitoneum.

to the discard of pneumoperitoneum but it is more likely to be related to the lack of change in antimicrobial regimens.

There is a closer relationship between the curve for the use of pneumoperitoneum and that for the average duration of hospital stay. The latter began to rise *pari passu* with the former and has shown some recent decline, probably because the patients feel that the therapeutic attack is now less active. Those who leave the hospital against medical advice (36 per cent) commonly reason that they can get the same rest, diet and antimicrobials at home. The use of pneumoperitoneum seems to be more

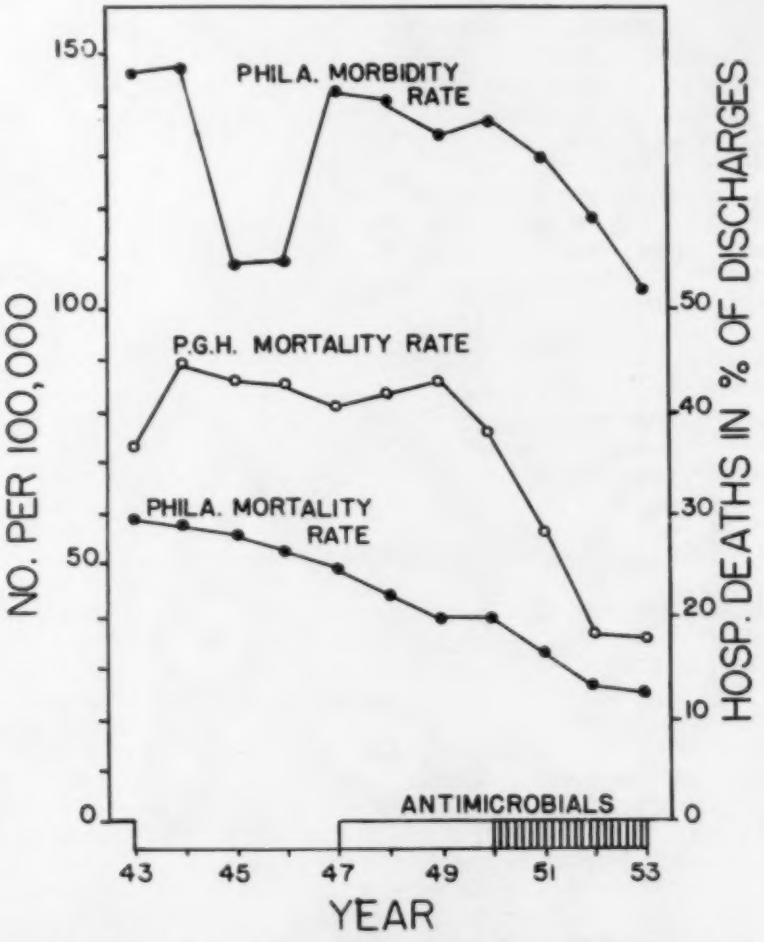

FIGURE 2: Curves for the tuberculosis morbidity and mortality rates of the city of Philadelphia and the hospital tuberculosis mortality rate correlated with the use of the antimicrobial drugs by year from 1943 to 1953 inclusive. The city rates are given as the number per 100,000 population and the hospital rate as the percentage of total discharges.

of a deterrant to leaving the hospital than injections of streptomycin.

From 1947 to 1950 antimicrobial therapy consisted of short courses of streptomycin, at first alone and later combined with PAS. This had no demonstrable effect on the mortality rate here although the United States Public Health Service was able to show a decrease in mortality with a 91 day course of streptomycin.[2] In 1950 combined drug therapy was gradually prolonged for increasing periods of time and the mortality rate began to fall. With the addition of isoniazid in 1952 the mortality rate continued to drop but in 1953, when there were no remarkable changes in antimicrobial regimens, the mortality rate remained the same. Since a large proportion of patients admitted to this institution are terminal, this is not surprising. Even potent drugs can not stave off death in near-moribund cases. It is probable that a mortality rate of 18 per cent of all discharges represents a figure close to rock bottom and it will not be susceptible to any effect of further advances in therapy as long as a percentage of admissions continue to be riddled with hopelessly extensive irreversible disease. Further, the cause of death is now more often non-tuberculous.

It is of interest to compare the hospital mortality rate with the tuberculosis morbidity and mortality rates for the entire city of Philadelphia.[3] In Figure 2 the latter two variables are presented as the number per 100,000 population. The morbidity rate is not reliable because it has varied greatly, depending on changes in the type of case reported as active tuberculosis and on changes in the zeal with which physicians were encouraged to report the disease. This accounts for the marked shifts in the morbidity rate between 1944 and 1947. After 1950 the morbidity rate began to drop more and more rapidly and this may be correlated with the use of prolonged combined drug regimens because many patients who left the hospital in recent years were rendered sputum negative even though they were not "cured." However, this drop in the number of new cases appearing in Philadelphia may be due to the effect of the law of diminishing returns as it applies to improved case finding.

The Philadelphia tuberculosis mortality rate has shown a gradual decline which became slightly accelerated during 1951 and 1952 when effective drug regimens came into use but the fall in the mortality for the city as a whole was by no means as remarkable as that noted within hospital walls. Since Philadelphia has an inadequate number of hospital beds for tuberculosis, the majority of hospitalized cases are those patients who are most urgently in need of isolation and treatment. This explains in part why the effect of present day therapy has been more dramatic among hospitalized patients than among tuberculous patients in the city as a whole. In addition, comparison of these death rate curves suggests the desirability of hospital care for the tuberculous because all therapeutic methods can be brought to bear at the proper time with greater effectiveness and convenience.

The mortality rate is a reliable index to the more immediate efficacy of therapeusis for a chronic disease like tuberculosis. The effect of the potent antimicrobials has been universally observed, particularly with respect to

the death rate of miliary and meningeal tuberculosis.[4] Future long range studies will indicate the degree of efficacy with which present regimens produce "cure" in those patients who survive the disease.

Addendum: Figures for 1954 compared to figures for 1953 show no further changes except for a further decrease in the use of pneumoperitoneum.

SUMMARY

There has been a sudden rapid decline in the tuberculosis mortality rate at the Philadelphia Hospital in the last few years. This is not due to the major therapies of rest, diet or pneumothorax nor to change in the type of patient treated. It may be related possibly to the use of pneumoperitoneum but is probably more closely related to the use of prolonged combined antimicrobial regimens including streptomycin, PAS and isoniazid. The use of pneumoperitoneum is more closely related to changes in the average duration of hospitalization.

The dramatic decline in the hospital mortality rate is not well reflected by the tuberculosis mortality rate for the city of Philadelphia, probably due to the lack of sufficient beds. This suggests, in part, that hospital care is desirable for the tuberculous patient.

RESUMEN

En los últimos pocos años ha habido una declinación rápida y repentina de la mortalidad por tuberculosis en el Hospital General de Filadelfia. Esto no se debe en su mayor parte a los tratamientos principales por reposo, dieta o por el neumotórax ni a un cambio en el tipo de enfermos tratados. Posiblemente puede tener relación con el uso del neumoperitoneo pero probablemente tiene más estrecha relación con el uso prolongado de regimenes antimicrobianos combinados incluyendo estreptomicina, PAS e isoniacida. El uso del neumoperitoneo está más estrechamente relacionado con los cambios en el término medio de laduración del internamiento.

La declinación dramática de la mortalidad en el hospital no está bien reflejada por la mortalidad tuberculosa en la ciudad de Filadelfia, probablemente debido a la falta de camas suficientes. Esto sugiere, en parte, que el cuidado hospitalario es deseable para el tuberculoso.

RESUME

Il y a eu un brusque et rapide déclin du taux de la mortalité tuberculeuse á l'Hôpital Général de Philadelphie ces quelques derniéres années. Ceci n'est pas attribuable aux traitements essentiels par le repos, le régime, le pneumothorax, ni aux changements de catégorie des malades traités. Ce phénoméne est peut-être lié á l'utilisation du pneumopéritoine, mais il est encore plus étroitement lié à l'usage des traitements antibiotiques prolongés et combinés, comprenant la streptomycine, le P.A.S. et l'isoniazide. Le pneumopéritoine a surtout amené des modifications de la durée moyenne d'hospitalisation.

Le déclin spectaculaire du taux de la mortalité à l'hôpital n'est pas exactement suivi par celui de la mortalité tuberculeuse dans la ville de Philadelphie, ce qui s'explique vraisemblablement par le manque de lits.

Ces constatations amènent à penser, dans une certaine mesure, que la séjour à l'hôpital s'impose pour traiter les tuberculeux.

ZUSAMMENFASSUNG

Es ist zu einem plötzlichen, jähen Abfall der Tuberkulose-mortalitätsziffer im Allgemeinen Krankenhaus von Philadelphia in den letztvergangenen Jahren gekommen. Dieser ist nicht zurückzuführen auf die vorwiegende Behandlungsformen von Ruhe, Diät oder Pneumothorax und auch nicht auf einen Wechsel in der Art der behandelten Kranken. Er kann möglicherweise bezogen werden auf die Anwendung des Pneumoperitoneums, aber wahrscheinlich steht er in näherer Beziehung zur Verwendung von verlängerter kombinierter antimikrobieller Verordnungsweise, die Streptomycin, PAS und INH umfasst. Die Benutzung des Pneumoperitoneums steht mehr im Zusammenhang zu der geänderten durchschnittlichen Dauer des Krankenhausaufenthaltes.

Der erregende Rückgang der Krankenhaus-Sterblichkeitsziffer wird nicht deutlich widergespiegelt in der Tuberkulose-Sterblichkeitsziffer für die Stadt Philadelphia selbst, wahrscheinlich infolge eines Mangels an ausreichenden Betten. Dies legt, wenigstens in gewisser Beziehung, die Vermutung nahe, dass die Krankenhausbehandlung für die tuberkulösen Patienten wünschenswert sei.

REFERENCES

1 Weiss, W.: "Impact of Modern Therapy on Pulmonary Tuberculosis in a Large Municipal Hospital," *J.A.M.A.*, 152:890, 1953.

2 Long, E. R. and Ferebee, S. H.: "A Controlled Investigation of Streptomycin Treatment in Pulmonary Tuberculosis," *Pub. Health Reports*, 65:1421, 1950.

3 From data provided by W. J. Carnahan, Research Secretary, Philadelphia Tuberculosis and Health Association.

4 13th Veterans Administration—Army-Navy Conference on Chemotherapy on Tuberculosis, St. Louis, Missouri, February 8-11, 1954.

The President's Page

Chicago, the metropolis of the Midwest, beautifully situated on the shores of Lake Michigan, will be host to the 22nd annual scientific assembly of the American College of Chest Physicians. The Hotel Sherman has been selected as headquarters for this important meeting and the dates are June 7-10. Members of the College in increasing numbers have been attending the outstanding scientific programs arranged by our energetic program committees and this year we are anticipating an even larger attendance. The excellent scientific program, arranged by Dr. William A. Hudson and his committee, is published in this issue of our journal.

I wish to call your attention to a few of the features which I am certain will be of interest to you. By special request, we are repeating the Fireside Conferences. If you did not attend the premiere of this novel and instructive part of the program in Atlantic City last year, it should be a *must* on your calendar this year. It is the largest informal discussion group ever assembled in one room; more than fifty experts will be available to discuss every phase of diseases of the chest with you. Congenial hosts will be on hand to greet and assist you in meeting the discussion leaders. Refreshments will be available to help liven the discussions.

The ever-popular round table luncheon meetings will again be featured at the meeting. You will be able to choose your favorite topics from six luncheon meetings each day.

Through the generosity of Mrs. Fanny Mark, the First Louis Mark Memorial Lecture will be presented on Thursday evening, June 7. Dr. Leroy E. Burney, Assistant Surgeon General, U. S. Public Health Service, will present this lecture and he has selected as his title "What Can the Public Health Service Contribute to the Private Practice of Medicine." This inaugural lecture will be followed by an interesting symposium on carcinoma in which a group of prominent experts will participate. On each succeeding day of the meeting I am sure you will find stimulating lectures, panels, symposia and discussions on most every aspect of chest diseases. An excellent group of motion pictures will be shown concurrently during each day of the scientific assembly.

The Executive Council, Board of Regents, Board of Governors, state chairmen of Membership Committees, and all of our councils and committees will meet during this annual session. I urge all of you who serve with these important bodies to be present and assist in formulating the policies and programs of the College.

On Saturday, June 9, another large class will be inducted as Fellows of the College at the Annual Convocation, to be followed by a cocktail party, the Presidents' Banquet and dancing. The College Medal will be awarded to an outstanding scientist on this occasion. This is always a most enjoyable evening and your wives are invited to attend these impressive ceremonies and social functions with you. It gives me a great deal of pleasure to announce that an Open House will be held on Sunday, June 10, at the College Building. I am sure that all of you will want to visit the attractive College Offices.

The Illinois Chapter of the College is the host organization for our meeting this year in Chicago. The physical arrangements for the meeting are under the direction of Dr. Otto L. Bettag, Regent of the College, and his efficient committees. An interesting program of ladies' activities is being organized by the Ladies Reception Committee, under the chairmanship of Mrs. Bettag.

I trust that you will remain in Chicago for the meeting of the American Medical Association, June 11-15, particularly so that you may attend the Section on Diseases of the Chest and its splendid exhibits. If you have not already made hotel reservations, please do so at once. You will find a coupon for this purpose on page 468.

Mrs. Stygall and I are looking forward to the pleasure of greeting you and your wife in Chicago.

James H. Stygall

SEMINARS

Hotel Sherman, Chicago

Wednesday, June 6

The following seminars on diseases of the chest will be presented at the Hotel Sherman on Wednesday, June 6, and are open to all physicians. The seminars have been accredited by the Board of Examiners for candidates for Fellowship in the College. The registration fee for each seminar, which consists of a series of five lectures, is $7.50. Registration must be made in advance and accompanied by the tuition fee; seating capacity is limited and reservations will be accepted in the order received. A coupon for this purpose will be found opposite page 471. Please indicate your preference by number.

Morning Sessions—9:00 a.m.—12:00 Noon

AM-1 Pulmonary Disease (Medical)

"Chemotherapy and Antibiotics"

"Tuberculosis"

Meyer R. Lichtenstein, Associate Clinical Professor of Medicine, University of Illinois College of Medicine; Medical Director, Municipal Tuberculosis Sanitarium, Chicago

"Nontuberculous Diseases of the Chest"

F. Edmund Donoghue, Department of Medicine, Mayo Clinic, Rochester, Minnesota

"Pulmonary Function Testing"

David W. Cugell, Director, Cardio-Pulmonary Laboratories, Department of Medicine, Northwestern University Medical School, Chicago

"Emphysema"

Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School; Attending Physician, Cook County Hospital, Chicago

"Bronchial Disease"

David B. Radner, Assistant Professor of Medicine, Chicago Medical School; Director, Chest Department, Michael Reese Hospital, Chicago

Question and Answer Period

AM-2 Cardiology (Surgical)

"Congenital Disease"

"Diagnosis"

Robert A. Miller, Assistant Attending Cardiologist, Children's Memorial Hospital; Instructor, Department of Pediatrics, Northwestern University Medical School, Chicago

"Treatment"

Egbert H. Fell, Clinical Professor of Surgery, University of Illinois College of Medicine, Chicago

"Acquired Valvular Disease"

Laurence H. Rubenstein, Associate in Thoracic Surgery, Chicago Medical School; Consultant, Thoracic Surgery, Illinois Department of Public Welfare

"Diseases of the Thoracic Aorta"

Ormand C. Julian, Clinical Associate Professor of Surgery, University of Illinois College of Medicine; Associate Attending Surgeon, St. Luke's Hospital, Chicago

"Coronary Disease"

S. Allen Mackler, Professor of Thoracic Surgery, Cook County Graduate School of Medicine; Assistant Professor of Thoracic Surgery, Chicago Medical School, Chicago

Question and Answer Period

Wednesday, June 6, Seminars (continued)

Afternoon Sessions—2:00 p.m.—5:00 p.m.

PM-1 Pulmonary Disease (Surgical)

"Pulmonary Resection"

"Tuberculosis"

William M. Lees, Clinical Assistant Professor of Surgery, Stritch School of Medicine, Loyola University; Chief of Surgical Service, Municipal Tuberculosis Sanitarium, Chicago

"Carcinoma"

Robert J. Jensik, Clinical Assistant Professor of Surgery, University of Illinois College of Medicine; Consulting Thoracic Surgeon, St. Joseph's Hospital, Chicago

"Suppuration"

Edward E. Avery, Associate in Surgery, Northwestern University Medical School, Chicago

"Mediastinal Surgery"

Hiram T. Langston, Associate Professor of Medicine, University of Illinois College of Medicine; Chief Surgeon, Chicago State Tuberculosis Sanitarium, Chicago

"Esophageal Surgery"

William E. Adams, Raymond Professor, Department of Surgery, University of Chicago School of Medicine, Chicago

Question and Answer Period

PM-2 Cardiology (Medical)

"Congenital Heart"

Benjamin Gasul, Clinical Professor of Pediatrics, University of Illinois College of Medicine; Director, Pediatric Cardio-physiology Department, Cook County Children's Hospital, Chicago

"Rheumatic Fever"

Chester M. Kurtz, Professor of Clinical Medicine, University of Wisconsin Medical School, Madison, Wisconsin

"Cardiac Catheterization"

Aldo A. Luisada, Director, Division of Cardiology, Chicago Medical School, Chicago

"Myocardial Infarction"

Chauncey C. Maher, Associate Professor of Medicine, Northwestern University Medical School; Professor of Medicine, Cook County Graduate School of Medicine, Chicago

"Cor Pulmonale"

Irving Mack, Clinical Assistant Professor of Medicine, Chicago Medical School; Research Associate, Cardiovascular Department, Michael Reese Hospital, Chicago

Question and Answer Period

MOTION PICTURE PROGRAM

"Methods of Replacement of the Tracheal and Bronchial Wall"
Osler A. Abbott, Emory University Hospital, Georgia

"Experimental Coronary Artery Ligation in Regard to Survival, Electrocardiogram and Serum Transaminase"
E. Grey Dimond, University of Kansas Medical Center, Kansas City, Kansas

"New Technic of Bronchoscopy"
J. M. Dubois de Montreynaud, R. J. Edwards and A. J. Gladu, Rheims, France

"Physiology and Pathology of Bronchial Obstruction"
Paul H. Holinger and Kenneth C. Johnson, Chicago, Illinois

"Action of Human Heart Valves"
Karl P. Klassen, University Hospital, Columbus, Ohio

"The Experimental Pathogenesis of Tuberculosis"
Robert H. Ebert and William R. Barclay, University of Chicago, Chicago, Illinois

"High Speed Motion Picture Photography in the Study of Congenital Heart Disease"
F. Mason Sones Jr., Chief, Cardiorespiratory Department, Cleveland Clinic, Cleveland, Ohio

SCIENTIFIC PROGRAM

Thursday, June 7

8:00 p.m.—Scientific Session

First Louis Mark Memorial Lecture

"What Can the Public Health Service Contribute to the Private Practice of Medicine"

Leroy E. Burney, Assistant Surgeon General, U. S. Public Health Service, Washington, D. C.

Symposium on Carcinoma

"Biological Aspects of Carcinoma"

Clarence Cook Little, Director, Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine; Chairman of the Board and Scientific Director, Tobacco Industry Research Committee

"Follow-up Report on the Serial Section Study of the Tracheobronchial Tree"

Oscar Auerbach, Chief, Laboratory Service, Veterans Administration Hospital, East Orange, New Jersey; Associate Professor of Pathology, New York Medical College, New York City; and **J. Brewster Gere**, Veterans Administration Hospital, East Orange, New Jersey

"A Clinical Appraisal of Pulmonary Cytology"

Seymour M. Farber, Associate Clinical Professor of Medicine, University of California School of Medicine, San Francisco, California

"Surgical Management of Carcinoma of the Lung"

Richard H. Overholt, Clinical Professor of Surgery, Tufts College Medical School; Thoracic Surgeon, New England Deaconess Hospital; Director, Overholt Thoracic Clinic; and **James Bougos**, Overholt Thoracic Clinic, Boston, Massachusetts

"Radiation Therapy in Carcinoma of the Lung"

David M. Gould, Professor and Head, Department of Radiology, University of Arkansas Medical School, Little Rock, Arkansas

Quizmasters:

Alfred Goldman, Chief of Professional Services, City of Hope Medical Center, Duarte; Chief of Thoracic and Cardiac Surgery, Cedars of Lebanon Hospital, Los Angeles, California

Edgar Mayer, Clinical Professor of Medicine, New York University Graduate School of Medicine, New York City

Coleman B. Rabin, Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Questions and Discussion from the floor

Friday, June 8

8:35 a.m.—Scientific Session

"Cardiovascular and Pulmonary Physiology"

Burgess L. Gordon, President and William J. Mullen Professor of Medicine, Woman's Medical College of Pennsylvania, Philadelphia

"Techniques for the Study of Pulmonary and Cardiovascular Physiology"

Ross Kory, Chief, Investigative Medicine, Veterans Administration Center, Wood, Wisconsin

"Normal Physiology of the Cardiovascular System"

James Kieran, Clinical Instructor in Medicine, Stanford University School of Medicine, Oakland, California

"Bronchitis, Bronchiolitis, Bronchial Obstruction and Asthma"

Maurice S. Segal, Clinical Professor of Medicine, Tufts College Medical School; Director, Department of Inhalation Therapy, Boston City Hospital, Boston, Massachusetts

Questions and discussion from the floor

Friday, June 8 (continued)

10:00 a.m.— Symposium on Congenital Cardiovascular Disease

Moderator:

Charles P. Bailey, Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Panel:

John W. Kirklin, Assistant Professor of Surgery, Mayo Foundation, University of Minnesota Medical School, Rochester, Minnesota

C. Walton Lillehei, Associate Professor Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

Questions and discussion from the floor

Report of the Committee on Cardiovascular Surgery: "Coarctation of the Aorta"
William R. Rumel, Associate Clinical Professor of Surgery and Chairman, Division of Thoracic Surgery, University of Utah School of Medicine, Salt Lake City

"Cross Plication of the Annulus Fibrosis for Correction of Mitral Insufficiency"
Henry T. Nichols, Instructor in Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

Questions and discussion from the floor

11:30 a.m.—Adjourn to visit exhibits

12:00 noon—Round Table Luncheon Discussions **(see page 463)**

2:00 p.m.—Scientific Session

Symposium on Pulmonary Fibrosis

"Industrial Pulmonary Fibrosis—Its Influence on the Pulmonary Circulation: Histo-pathological Aspects"
Gerritt W. H. Schepers, Director, The Saranac Laboratory, Saranac Lake, New York

"Fibrosis and Its Relation to Radiation"
Major General James P. Cooney, Deputy Surgeon General, Department of the Army, Washington, D. C.

"The Heart and Circulatory Mass in Pulmonary Diseases"
George R. Herrmann, Professor of Internal Medicine; Director, Cardiovascular Research Laboratory; Director, Heart Station, University of Texas Medical Branch, Galveston, Texas

Questions and discussion from the floor

"Why Not a Modern Replacement for Our Antiquated Stethoscope?"
Oliver E. Turner, Mercy Hospital, Pittsburgh, Pennsylvania

"Alaskan Adventure—Radiography in the Arctic"
Charles T. Dotter, Professor and Head, Department of Radiology, University of Oregon Medical School, Hospitals and Clinics, Portland, Oregon

"Osseous Tuberculosis with Concurrent Pulmonary Lesions"
Harry Fisher, Associate Orthopedic Surgeon, Presbyterian and Woman's Hospitals, Pittsburgh, Pennsylvania

"Asymptomatic Primary Tuberculosis"
Edwin L. Kendig, Jr., Consultant, Chest Diseases in Children, Richmond, Virginia

Questions and discussion from the floor

4:30 p.m.—Adjourn to visit exhibits

Friday, June 8 (continued)

8:15 p.m.—Scientific Session

"Fireside Conferences"
Subjects and Discussion Leaders

"Emphysema"

Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Peter A. Theodos, Associate in Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

"Immunity and Vaccination in Tuberculosis"

Robert J. Anderson, Assistant Chief, Division of Special Health Services, U. S. Public Health Service, Washington, D. C.

Jay Arthur Myers, Professor of Medicine and Public Health, University of Minnesota Medical and Graduate Schools, Minneapolis, Minnesota

"Bronchoesophagology"

Chevalier L. Jackson, Professor and Head, Department of Laryngology and Bronchoesophagology, Temple University School of Medicine, Philadelphia, Pennsylvania

George S. McReynolds, Associate Professor of Otolaryngology, University of Texas School of Medicine, Galveston, Texas

"Surgery of the Heart Valves"

Ralph A. Deterling, Associate Clinical Professor of Surgery, Columbia University College of Physicians and Surgeons, New York City

Robert P. Glover, Clinical Professor of Thoracic Surgery, Hahnemann Medical College, Philadelphia, Pennsylvania

"Angiocardiography"

Elmer C. Rigby, Consultant in Thoracic Surgery, State of California, Los Angeles, California

Leo G. Rigler, Professor and Chief, Department of Radiology, University of Minnesota (on leave of absence); (temporarily) Chief, Department of Radiology and Director, Postgraduate Medical Education, City of Hope Medical Center, Duarte; Visiting Professor, Department of Radiology, University of California, Los Angeles, California

Israel Steinberg, Assistant Clinical Professor of Medicine and Radiology, Cornell University Medical College, New York City

"Pathology of Resected Lesions"

Emil Bogen, Clinical Professor, Department of Infectious Diseases, University of California School of Medicine, Los Angeles, California

Henry C. Sweany, Director of Research, Pathology and Allied Sciences, Missouri State Sanatorium, Mount Vernon, Missouri

"Pressure Breathing"

Hurley L. Motley, Professor of Medicine and Director, Cardio-Respiratory Laboratory, University of Southern California, Los Angeles, California

Frank Princi, Associate Professor of Industrial Medicine, University of Cincinnati College of Medicine; Assistant Director, University of Cincinnati Institute of Industrial Health, Cincinnati, Ohio

"Excision in Tuberculosis"

J. Maxwell Chamberlain, Associate in Surgery, Columbia University College of Physicians and Surgeons, New York City

John B. Grow, Assistant Professor of Surgery, Colorado University School of Medicine, Denver, Colorado

Friday, June 8, Fireside Conferences (continued)

"Cardiac Function"

William B. Bean, Professor and Head, Department of Internal Medicine, State University of Iowa School of Medicine, Iowa City, Iowa

Gertrude H. Nicolson, Chief, Children's Cardiac Clinic, St. Luke's Hospital, New York City

"Asthma in Children"

Bret Ratner, Professor of Clinical Pediatrics and Head of Pediatric Allergy, New York Medical College, New York City

Leon Unger, Associate Professor of Medicine, Northwestern University Medical School, Chicago, Illinois

"Coronary Artery Disease—Surgery"

Charles P. Bailey, Professor and Head, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

William R. Rumel, Associate Clinical Professor of Surgery and Chairman, Division of Thoracic Surgery, University of Utah School of Medicine, Salt Lake City, Utah

David H. Waterman, Chief, Thoracic Surgery, Fort Sanders Presbyterian Hospital, Knoxville, Tennessee

"Pulmonary Function"

George R. Meneely, Associate Professor of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

Gerritt W. H. Schepers, Director, The Saranac Laboratory, Saranac Lake, New York

"Dust Diseases"

Howard S. Van Ordstrand, Assistant Professor of Medicine, Frank E. Bunts Educational Institute, Cleveland, Ohio

Arthur J. Vorwald, Professor and Chairman, Department of Industrial Medicine, Wayne University College of Medicine, Detroit, Michigan

"Rheumatic Heart Disease"

Harry Goldberg, Assistant Professor of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania

George A. Hellmuth, Chief of Cardiology, Marquette University School of Medicine, Milwaukee, Wisconsin

"Pathological Aspects and Differential Diagnosis of Fungus Infections of the Lung"

John F. Fennessey, Pathologist, Metropolitan and St. Joseph Hospitals, Detroit, Michigan

Michael L. Furcolow, Associate Clinical Professor of Medicine, University of Kansas School of Medicine, Kansas City, Kansas

Clarence I. Owen, Clinical Associate Professor of Pathology, Wayne University College of Medicine; Attending Pathologist and Director of Laboratories, Grace Hospital, Detroit, Michigan

"Bronchiectasis"

Arthur M. Olsen, Associate Professor of Medicine, Mayo Foundation, University of Minnesota Medical School, Rochester, Minnesota

Lawrence A. Pratt, Attending Thoracic Surgeon, Grace, Detroit Memorial, and Chest and General Hospitals, Detroit, Michigan

"Inoperable Carcinoma of the Lung"

Clyde K. Hasley, Clinical Assistant Professor of Radiology, Wayne University College of Medicine, Detroit, Michigan

Edgar Mayer, Clinical Professor of Medicine, New York University Graduate School of Medicine, New York City

Friday, June 8, Fireside Conferences (continued)

"Cor Pulmonale"

Stephen Elek, Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California

David Nafe Kerr, Instructor in Medicine, Washington University School of Medicine, St. Louis, Missouri

"Chemotherapy"

Winthrop N. Davey, Associate Professor of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan

Edward Dunner, Chief, Training and Standards, Tuberculosis Service, Veterans Administration, Washington, D. C.

"Esophageal Management"

Reuben I. Shapiro, Surgeon, Detroit Chest and General Hospital, Detroit, Michigan

Phillip Thorek, Clinical Associate Professor of Surgery, University of Illinois College of Medicine, Chicago, Illinois

"Rehabilitation in Cardiac Disease"

Norman E. Clarke, Associate Chief, Cardiorespiratory Division, Henry Ford Hospital, Detroit, Michigan

Nathaniel E. Reich, Assistant Professor of Clinical Medicine, State University of New York College of Medicine, Brooklyn, New York

"Fungus Disease"

Bert H. Cotton, Chief, Thoracic Surgery, Orange County Hospital, Los Angeles, California

Coleman B. Rabin, Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

"Congenital Heart Disease"

Daniel F. Downing, Associate Professor of Pediatrics, Hahnemann Medical College, Philadelphia, Pennsylvania

Paul F. Dwan, Clinical Associate Professor of Pediatrics, University of Minnesota, Minneapolis, Minnesota

"Collapse Therapy"

Arnold Minnig, Staffs, St. Luke's and Presbyterian Hospitals, Denver, Colorado

Jack Reiss, Chief, Chest Service, Veterans Administration Hospital, Coral Gables, Florida

"Surgery in Lung Tumors"

Lawrence H. Strug, Clinical Professor of Surgery, Louisiana State University School of Medicine, New Orleans, Louisiana

John V. Thompson, Thoracic Surgeon, Methodist Hospital, Indianapolis, Indiana

"Ambulatory Treatment in Tuberculosis"

Carl C. Aven, Staffs, Georgia Baptist and Piedmont Hospitals, St. Joseph's Infirmary, Atlanta, Georgia

Albert M. Wehenkel, Medical Director, Wehenkel Clinic, Detroit, Michigan

"Rehabilitation in Pulmonary Disease"

John H. Aldes, Director, Department of Rehabilitation, Cedars of Lebanon Hospital, Los Angeles, California

Clifford F. Storey, Capt., USN, U. S. Naval Hospital, San Diego, California

NOTE

These conferences are informal and offer an opportunity for free discussion of many subjects of interest to our members. Discussion Leaders will be seated at tables with proper identification. Physicians may participate in the discussion of their choice, or move on to other discussions when and if they desire. Refreshments will be available to enhance good fellowship.

Saturday, June 9

10:00 a.m.—Scientific Session, Section I

Symposium on Acquired Cardiovascular Disease

"Pathology of Acquired Valvular Disease—Hemodynamic Significance of Anatomic Variations"

Dwight E. Harken, Associate Clinical Professor of Surgery, Harvard University Medical School; Surgeon, Peter Bent Brigham Hospital, Boston, Massachusetts

"Selection of Patients for Surgical Intervention in Acquired Valvular Disease"

Laurence B. Ellis, Associate Clinical Professor of Medicine, Harvard University Medical School, Boston, Massachusetts

"The Surgical Correction of Acquired Valvular Defects"
Dwight E. Harken

"The Results of Surgical Correction of Acquired Valvular Disease from a Long Term Follow-up"
Laurence B. Ellis

Questions and discussion from the floor

11:30 a.m.—Adjourn to visit exhibits

10:00 a.m.—Scientific Session, Section II

"Clinical Importance of Dealing with Personality Aspects of the Tuberculous"

P. J. Sparer, Assistant Professor of Preventive Medicine, University of Tennessee College of Medicine; Chief, Psychiatry and Psychosomatics, Veterans Administration Hospital, Memphis; and **Neil W. Shelton**, Ph.D., Department of Psychiatry and Psychosomatics, Veterans Administration Hospital, Memphis, Tennessee

"New Trends in the Chemotherapy of Tuberculosis"

Colonel James A. Wier, Chief, Pulmonary Disease Section, Fitzsimons Army Hospital, Denver, Colorado

"Cyanacethydrazide in Pulmonary Tuberculosis"

Jacob J. Kirshner, Associate in Medicine, Jefferson Medical College, Philadelphia; Medical Director, Eagleville Sanatorium, Eagleville, Pennsylvania

"Apico-Osteoplasty: A Modified Thoracoplasty Technique"

Mauricio Goldberg, George Heitzman and **John B. Grow**, National Jewish Hospital, Denver, Colorado

Questions and discussion from the floor

11:30 a.m.—Adjourn to visit exhibits

12:00 noon—Round Table Luncheon Discussions **(see page 464)**

2:00 p.m.—Scientific Session, Section I

Symposium on Fungus Diseases

"The Medical Aspects of the Diagnosis and Treatment of Fungus Diseases"

Alvis E. Greer, Clinical Professor of Medicine, Baylor University College of Medicine, Houston, Texas

"Histoplasmosis"

Michael L. Furcolow, Associate Clinical Professor of Medicine, University of Kansas School of Medicine; Medical Director and Medical Officer in Charge, University of Kansas Medical Center, Kansas City, Kansas

"Blastomycosis"

John H. Seabury, Associate Professor of Medicine, Louisiana State University School of Medicine; Director, Lung Station, Charity Hospital, New Orleans

"Coccidioidomycosis—Clinical and Roentgen-ray"

Bert H. Cotton, Chief, Thoracic Surgery, Orange County Hospital; Attending Staff, Hollywood Presbyterian and Los Angeles County Hospital, Los Angeles

Questions and discussion from the floor

4:00 p.m.—Adjourn to visit exhibits

Saturday, June 9 (continued)

2:00 p.m.—Scientific Session, Section II

"Surgical Treatment of Pulmonary Tuberculosis"
Thomas J. Kinsella, Consultant in Thoracic Surgery, U. S. Veterans Bureau, Minnesota State Sanatorium, Glen Lake Sanatorium, Minneapolis General Hospital, North Dakota State Sanatorium, Mount Sinai Hospital, Minneapolis

"Experience with Intrathoracic Tailoring of the Pleural Cavity Following Partial Pulmonary Resection"
Robert Klopstock, Clinical Associate Professor of Surgery, State University Medical Center, Brooklyn; Chief, Thoracic Surgery, Veterans Administration Hospital, Brooklyn, New York

"Constrictive Pericarditis"
David Rutledge and **Robert Foley,** Department of Internal Medicine, Lahey Clinic, Boston, Massachusetts

"Present Trends in Chemotherapy of Pulmonary Tuberculosis in Great Britain"
Martin Nagley, Grove Park Hospital, Lee, England

"Changing Concepts in the Rehabilitation of the Tuberculous"
Sidney H. Dressler, Assistant Clinical Professor of Medicine, University of Colorado School of Medicine; Medical Director, National Jewish Hospital, Denver

Questions and discussion from the floor

4:00 p.m.—Adjourn to visit exhibits

Sunday, June 10

8:55 a.m.—Scientific Session

Symposium on Hypertension

"Non-Specific Myocardial Disease"
Louis F. Bishop, Assistant Clinical Professor of Medicine, New York University Postgraduate Medical School, Bellevue Medical Center; and **Gerard Gros,** New York University Medical School, New York City

"What is Hypertension in Older People?"
Arthur M. Master, Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons; Cardiologist, Mt. Sinai Hospital, New York City

"The Incidence of Congenital Malformations of the Heart in Hospital and Private Consultation Practice"
Benjamin M. Gasul, Clinical Associate Professor of Pediatrics, University of Illinois School of Medicine; Director, Cardio-physiology Department, Cook County Children's Hospital, Chicago, Illinois

"The Fate of the Implanted Internal Mammary Artery in Human Ischemic Hearts"
Arthur M. Vineberg and **G. C. McMillan,** Department of Pathology and Surgery, Royal Victorian Hospital, Montreal, Canada

"The Effect of Cardiac Arrhythemias on the Coronary Flow"
Eliot Corday, Department of Medicine, University of California; Chief, Cardiac Clinic, Cedars of Lebanon Hospital, Los Angeles, California

"The Problem of the Heart in Kyphoscoliosis"
George S. Bond, Professor Emeritus, Department of Cardiology, Indiana University School of Medicine, Indianapolis, Indiana

Questions and discussion from the floor

Sunday, June 10 (continued)

10:30 a.m.—

"Objective Data Regarding the Value of Denervation Surgery in the Treatment of Pulmonary Hypertrophic Emphysema"

Osler A. Abbott, Assistant Professor of Surgery, Chief, Division of Thoracic Surgery, Emory University Clinic and School of Medicine, Emory University, Georgia

"Report on Investigations Regarding the Common Cold"

Thomas G. Ward, Associate Professor of Microbiology, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, Maryland

"Experimental and Clinical Effects of Atmospheric Pollutants on the Respiratory System"

Paul Kotin, Associate Professor of Pathology, University of Southern California School of Medicine; Attending Pathologist, Los Angeles County General Hospital, Los Angeles, California

Questions and discussion from the floor

11:30 a.m.—Adjourn to visit exhibits

12:00 noon—Round Table Luncheon Discussions **(see page 465)**

2:00 p.m.—Scientific Session

"Combined Cycloserine Therapy in the Treatment of Pulmonary Tuberculosis"

Israel G. Epstein, Associate Clinical Professor of Medicine, New York Medical College; Assistant Director of Tuberculosis, Metropolitan Hospital; **K. G. S. Nair** and **Linn J. Boyd,** Department of Medicine, New York Medical College and Tuberculosis Division, Metropolitan Hospital, New York City

Questions and discussion from the floor

Symposium on Coronary Artery Disease

2:30 p.m.—

"Anatomical and Physiological Considerations in the Development of a Collateral Circulation to the Myocardium"

Frederick R. Mautz, Staff Associate, Beck Cardiovascular Research Laboratory; Surgeon, University Hospitals of Cleveland; Surgical Consultant, U. S. Public Health Service, Cleveland, Ohio

"Selection of Patients and Results of Operation"

Bernard L. Brofman, Director, Cardiovascular Research, Mt. Sinai Hospital, Cleveland, Ohio

"Myocardial Re-Vascularization" (including film)

Claude S. Beck, Professor of Cardiovascular Surgery, Western Reserve University and Hospitals; Director, Beck Cardiovascular Research Laboratory, Cleveland, Ohio

Questions and discussion from the floor

Adjournment

Committee on Scientific Program

William A. Hudson, Detroit, Michigan, Chairman
Albert H. Andrews, Chicago, Illinois, Vice-Chairman
Burgess L. Gordon, Philadelphia, Pennsylvania
Paul H. Holinger, Chicago, Illinois
Fay A. LeFevre, Cleveland, Ohio
Coleman B. Rabin, New York, N. Y.
David Salkin, San Fernando, California

ROUND TABLE LUNCHEONS

Friday, June 8

A-1 ***Chronic Dyspneic Diseases: Cardiac and Pulmonary Function Testing***

Hurley L. Motley, Professor of Medicine and Director, Cardio-Respiratory Laboratory, University of Southern California, Los Angeles, California

Frank Princi, Associate Professor of Industrial Medicine, University of Cincinnati College of Medicine; Assistant Director, University of Cincinnati Institute of Industrial Health, Cincinnati, Ohio

Joseph F. Tomashefski, Assistant Professor of Medicine, Ohio State University College of Medicine, Columbus; Staff, Ohio Tuberculosis Hospital, Columbus, Ohio

Moderator: **George R. Meneely**, Associate Professor of Medicine, Vanderbilt University School of Medicine; Director, Research Laboratory and Radioisotope Unit, Veterans Administration Hospital, Nashville, Tennessee

A-2 ***Tuberculosis: Epidemiology and Management of Recent Converters***

Otto L. Bettag, Director, Department of Public Welfare, State of Illinois, Chicago, Illinois

Benjamin L. Brock, Medical Director, Central Florida Tuberculosis Hospital, Orlando, Florida

Carl H. Gellenthien, Medical Director, Valmora Sanatorium, Valmora, New Mexico

Irving W. Willner, Director, Chest Disease Division, Department of Health, Newark, New Jersey

Moderator: **W. Leonard Howard**, Medical Director, William H. Maybury Sanatorium, Northville, Michigan

A-3 ***Thoracic Surgery: Circumscribed Lesions***

Osler A. Abbott, Assistant Professor of Surgery; Chief, Division of Thoracic Surgery, Emory University Clinic and School of Medicine, Emory University, Georgia

Richard H. Meade, Senior Attending Chest Surgeon, Butterworth Hospital; Consulting Chest Surgeon, Blodgett Memorial and St. Mary's Hospitals, Grand Rapids, Michigan

Moderator: **Alfred Goldman**, Chief of Professional Services, City of Hope Medical Center, Duarte; Chief of Thoracic and Cardiac Surgery, Cedars of Lebanon Hospital, Los Angeles, California

A-4 ***Coronary Disease***

Simon Dack, Lecturer in Medicine, Columbia University College of Physicians and Surgeons; Chief, Cardiac Clinic, Mt. Sinai Hospital, New York City

Alexander Libow, Associate Attending Physician, Diseases of the Chest, Mt. Sinai Hospital, Miami Beach, Florida

William Likoff, Associate Professor of Medicine, Hahnemann Medical College; Cardiologist, Bailey Thoracic Clinic, Philadelphia, Pennsylvania

Moderator: **John F. Briggs**, Associate Professor of Clinical Medicine, University of Minnesota Medical School, Minneapolis, Minnesota

A-5 ***Pulmonary Disease: Nonspecific Infections***

Winthrop N. Davey, Associate Professor of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan

Sol Katz, Adjunct Clinical Professor of Medicine, Georgetown University School of Medicine and George Washington Medical School, Washington, D. C.

Henry J. Stanford, Surgical Staff, Tucson Medical Center, Tucson, Arizona

Moderator: **Alfred Goldman**, Associate Professor of Clinical Medicine, Washington University School of Medicine, St. Louis, Missouri

A-6 ***Cardiac Disease: Rheumatic Fever***

Coleman B. Rabin, Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City

Gene H. Stollerman, Assistant Professor of Medicine, Northwestern University Medical School, Chicago, Illinois

Moderator: **Norman E. Clarke**, Attending Physician and Chairman, Department of Research, Providence Hospital; Associate Chief, Cardiorespiratory Division, Henry Ford Hospital, Detroit, Michigan

Round Table Luncheons (continued)

Saturday, June 9

B-1 ***Chronic Dyspneic Diseases: Physiologic Treatment***

Maurice S. Segal, Clinical Professor of Medicine, Tufts Medical College; Director, Department of Inhalation Therapy, Boston City Hospital, Boston, Massachusetts

Roger H. L. Wilson, Clinical Instructor in Medicine, University of California Medical Center, San Francisco, California

George W. Wright, Head, Department of Medical Research, St. Luke's Hospital, Cleveland, Ohio

Moderator: **Alvan L. Barach**, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons; Attending Physician, Presbyterian Hospital, New York City

B-2 ***Tuberculosis: Management of Residual Cavities***

James L. Mudd, Associate Clinical Professor and Chairman, Section on Thoracic Surgery, St. Louis University School of Medicine, St. Louis, Missouri

David H. Waterman, Chief, Thoracic Surgery, Fort Sanders Presbyterian Hospital; Attending Thoracic Surgeon, East Tennessee Tuberculosis Hospital, General Hospital, Knoxville, Tennessee

Moderator: **Willard B. Howes**, Medical Director, Chest and General Hospital, Detroit, Michigan

B-3 ***Thoracic Surgery: Bronchogenic Carcinoma***

Otto C. Brantigan, Professor of Thoracic Surgery and Surgical Anatomy, University of Maryland School of Medicine, Baltimore, Maryland

Edgar W. Davis, Professor of Thoracic Surgery, Georgetown University School of Medicine, Washington, D. C.

Alton Ochsner, The William Henderson Professor of Surgery and Chairman, Department of Surgery, Tulane University, Louisiana School of Medicine; Director, Section on Surgery, Ochsner Clinic and Foundation Hospital, New Orleans

Clifford F. Storey, Capt., USN, U. S. Naval Hospital, San Diego, California

Moderator: **Jerome R. Head**, Assistant Professor of Surgery, Northwestern University Medical School, Chicago; Medical Director, Edward Sanitarium, Naperville, Illinois

B-4 ***Congenital Anomalies of the Lung***

Charles T. Dotter, Professor and Head, Department of Radiology, University of Oregon Medical School, Hospitals and Clinics, Portland, Oregon

William L. Riker, Associate Attending Surgeon, Children's Memorial and Grant Hospitals, Chicago, Illinois

Moderator: **James A. Wier**, Col., Chief, Pulmonary Disease Service, Fitzsimons Army Hospital, Denver, Colorado

B-5 ***Pulmonary Disease: Fungus Infections***

Benson Bloom, Staff, Tucson Medical Center and St. Mary's Hospital and Sanatorium, Tucson, Arizona

Bert H. Cotton, Chief, Thoracic Surgery, Orange County Hospital; Attending Staff, Hollywood Presbyterian Hospital, Los Angeles County Hospital, Los Angeles, California

Alvis E. Greer, Clinical Professor of Medicine, Baylor University College of Medicine, Houston, Texas

Moderator: **Andrew L. Banyai**, Associate Clinical Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin

B-6 ***Cardiac Disease: Hypertension***

Stephen Elek, Assistant Clinical Professor of Medicine, University of Southern California School of Medicine; Chief, Cardiac Clinic, Cedars of Lebanon Hospital, Los Angeles, California

M. Jay Flipse, Chief, Medical Service, Dade County Hospital; Chief, Tuberculosis Service, Jackson Memorial Hospital, Miami, Florida

Maurice A. Schnitker, Director of Medicine and Chief of Medical Service, St. Vincent Hospital, Toledo, Ohio

Moderator: **Walter S. Priest**, Associate Professor of Medicine, Northwestern University Medical School; Senior Attending Physician, Wesley Memorial Hospital, Chicago, Illinois

Round Table Luncheons (continued)

Sunday, June 10

C-1 *Chronic Dyspneic Diseases: Allergic Aspects*

Harry L. Rogers, Assistant Professor of Clinical Medicine, Jefferson Medical College; Physician-in-Charge, Allergy Out-Patient Department, Jefferson Hospital, Philadelphia, Pennsylvania

Clarence S. Thomas, Associate Professor of Clinical Medicine, Vanderbilt University School of Medicine

Moderator: **Leon Unger**, Associate Professor of Medicine, Northwestern University Medical School; Attending Physician, Cook County Hospital, Chicago, Illinois

C-2 *Tuberculosis: New Aspects of Chemotherapy*

Meyer R. Lichtenstein, Associate Clinical Professor of Medicine, University of Illinois College of Medicine; Medical Director, Municipal Tuberculosis Sanitarium, Chicago, Illinois

Charles E. Lyght, Associate Medical Director, Merck & Company, Inc., Rahway, New Jersey

Henry C. Sweany, Director of Research, Pathology and Allied Sciences, Missouri State Sanatorium, Mount Vernon, Missouri

Moderator: **Karl H. Pfuetze**, Clinical Professor of Medicine, University of Illinois College of Medicine; Medical Director, Chicago State Tuberculosis Sanitarium, Chicago, Illinois

C-3 *Thoracic Surgery: Esophageal Carcinoma*

Arthur J. Cracovaner, Clinical Professor of Otorhinolaryngology, Postgraduate Medical School, New York University-Bellevue Medical Center, New York City

Karl P. Klassen, Professor and Head, Department of Thoracic Surgery, Ohio State University College of Medicine, Columbus, Ohio

Moderator: **William E. Adams**, Raymond Professor, Department of Surgery, University of Chicago School of Medicine, Chicago, Illinois

C-4 *Septal Defects and Lung-Heart Machines*

Forest D. Dodrill, Surgeon, Harper Hospital; Attending Surgeon, Providence Hospital, Detroit, Michigan

C. Walton Lillehei, Associate Professor of Surgery, The Medical School, University of Minnesota, Minneapolis, Minnesota

Moderator: **John B. Kirklin**, Assistant Professor in Surgery, Mayo Foundation, University of Minnesota, Rochester, Minnesota

C-5 *Pulmonary Disease: Industrial Dust Disease*

Oscar A. Sander, Associate in Medicine, Marquette University Medical School, Milwaukee County Hospital and Columbia Hospital, Milwaukee, Wisconsin

Eugene L. Walsh, Assistant Professor of Medicine, Northwestern University Medical School; Medical Director International Harvester Corporation, Chicago, Illinois

Moderator: **Arthur J. Vorwald**, Professor and Chairman, Department of Industrial Medicine, Wayne University College of Medicine, Detroit, Michigan

C-6 *Cardiac Disease: Pulmonary Edema*

William P. Chester, Staff, Providence Hospital, Detroit, Michigan

Aldo A. Luisada, Director, Division of Cardiology, Chicago Medical School, Chicago, Illinois

Moderator: **George R. Herrmann**, Professor of Internal Medicine; Director, Cardiovascular Research Laboratory; Director, Heart Station, University of Texas Medical Branch, Galveston, Texas

ADMINISTRATIVE SESSIONS

Wednesday, June 6

8:00 a.m.—Committee on Seminars
10:00 a.m.—Committee on By-Laws
12:00 noon—Luncheon, Executive Council
2:30 p.m.—Board of Regents

Thursday, June 7

9:00 a.m.—Joint Meeting, Board of Governors and Board of Regents
9:00 a.m.—Committee on Occupational Diseases of the Chest
9:00 a.m.—Committee on Resident Fellowships
9:00 a.m.—Committee on Scientific Program
9:00 a.m.—Cardiovascular Committee Sections
- Clinical Cardiovascular Disease
- Therapy
- Cardiovascular Physiology
- Electrocardiography
- Roentgenology
- Cardiovascular Surgery
- Pediatric Cardiology
- Rehabilitation

9:30 a.m.—Board of Examiners
10:00 a.m.—Committee on Membership
10:30 a.m.—Committees of the Council on Undergraduate Medical Education
- Committee on Undergraduate Medical Education
- Committee on Motion Pictures
- Committee on Audiovisual Aids
- Committee on College Essay Award

10:30 a.m.—Council on Postgraduate Medical Education
10:30 a.m.—Council on Public Health
- Committee on Indian Affairs
- Committee on Liaison with State and County Medical Societies

10:30 a.m.—Committees of the Council on Research
- Committee on Non-Surgical Therapy
- Committee on Pulmonary Surgery
- Committee on Bronchoesophagology
- Committee on Chemotherapy and Antibiotics
- Committee on Physiologic Therapy
- Committee on Allergy
- Committee on Microbiology

10:30 a.m.—Committees of the Council on Hospitals
- Committee on Standards and Accreditation
- Committee on Rehabilitation
- Committee on Chest Diseases in Institutions
- Committee on Psychosomatic Aspects of Diseases of the Chest

12:00 noon—**LUNCHEON, 12TH ANNUAL COLLEGE CONFERENCE**
(Open to all members of the College)
James H. Stygall, Indianapolis, Indiana, President, presiding

Awarding of Certificates of Merit to Past-Presidents of College Chapters

GROWTH AND DEVELOPMENT OF THE COLLEGE
Chevalier L. Jackson, Chairman, Committee on Membership, Philadelphia

2:00 p.m.—Joint Meeting
- Council on Hospitals
- Committee on Standards and Accreditation
- Committee on Rehabilitation
- Committee on Chest Diseases in Institutions
- Committee on Psychosomatic Aspects of Diseases of the Chest

2:00 p.m.—Joint Meeting
- Council on Research
- Committee on Non-Surgical Therapy
- Committee on Pulmonary Surgery
- Committee on Bronchoesophagology
- Committee on Chemotherapy and Antibiotics
- Committee on Physiologic Therapy
- Committee on Allergy
- Committee on Microbiology

Thursday, June 7, Administrative Sessions (continued)

2:00 p.m.—Joint Meeting
Council on Undergraduate Medical Education
Committee on Undergraduate Medical Education
Committee on Motion Pictures
Committee on Audiovisual Aids
Committee on College Essay Award
2:00 p.m.—Council on Postgraduate Medical Education
2:00 p.m.—Joint Meeting
Council on Public Health
Committee on Indian Affairs
Committee on Liaison with State and County Medical Societies
3:00 p.m.—Committee on College Chapters
4:00 p.m.—Committee on Insurance
4:00 p.m.—**OPEN FORUM, COUNCIL ON HOSPITALS**
Charles A. Brasher, Mt. Vernon, Missouri, Chairman, presiding

ACCREDITATION OF TUBERCULOSIS HOSPITALS
Kenneth B. Babcock, Director, Joint Commission on Accreditation of Hospitals, Chicago, Illinois

Questions and discussion from the floor

Friday, June 8

2:00 p.m.—Committee on Nominations
3:00 p.m.—Editorial Board
4:00 p.m.—Joint Meeting
Committee on Chemotherapy and Antibiotics
Committee on Physiologic Therapy
Committee on Antimicrobials
4:00 p.m.—Joint Meeting
Committee on Chest Diseases in Institutions
Committee on Psychosomatic Aspects of Diseases of the Chest
4:00 p.m.—Committee on College Lectureships

Saturday, June 9

9:00 a.m.—Open Administrative Session
Report of the Historian
Report of the Treasurer
Report of the Executive Director
Report of the Committee on Nominations
Election of Officers

Sunday, June 10

8:00 a.m.—Past-Presidents' Breakfast
2:00 p.m.—Board of Regents

SOCIAL ACTIVITIES

Saturday, June 9

6:00 p.m.—Annual Convocation (Formal)
7:00 p.m.—Cocktail Party
Sponsored by The Panray Corp., New York City
7:30 p.m.—Annual Presidents' Banquet
9:30 p.m.—After-Dinner Dancing

Sunday, June 10

5:00 p.m.—Open House
College Building
112 East Chestnut Street

LADIES ACTIVITIES

The Ladies Reception Committee is planning some special functions for the ladies which will be announced in the near future. Mrs. Otto L. Bettag, Chicago, is serving as the Chairman of the committee.

TECHNICAL EXHIBITORS

V. Ray Bennett and Associates, Inc.
Los Angeles, California
Warren E. Collins, Inc.
Boston, Massachusetts
Duncan Oxygen Therapy Company
Duncan, Oklahoma
Eliot Medical Plastics Company
Lynn, Massachusetts
J. H. Emerson Company
Cambridge, Massachusetts
E. Fougera and Company, Inc.
New York, New York
Grune & Stratton, Inc.
New York, New York
Hellwig Laboratories, Inc.
Chicago, Illinois
Instrumentation Associates, Inc.
New York, New York
Irwin, Neisler and Company, Inc.
Decatur, Illinois
Eli Lilly and Company, Inc.
Indianapolis, Indiana
Linde Air Products Company
New York, New York
S. E. Massengill Company, Inc.
Bristol, Tennessee
Micro X-ray Recorder Company
Chicago, Illinois
Mine Safety Appliances Company
Pittsburgh, Pennsylvania
Mist O_2 Gen Equipment Company
Oakland, California
J. J. Monaghan Company
Denver, Colorado
Oxygen Equipment Manufacturing Co.
St. Louis, Missouri
Ohio Chemical & Surgical Equipment Co.
Madison, Wisconsin
The Panray Corporation
New York, New York
Chas. Pfizer and Company, Inc.
Brooklyn, New York
George P. Pilling & Son Company
Philadelphia, Pennsylvania
W. B. Saunders Company
Philadelphia, Pennsylvania
Schering Corporation
Bloomfield, New Jersey
Sharp & Dohme
Philadelphia, Pennsylvania
Charles C Thomas, Publisher
Springfield, Illinois
Vaponefrin Company
Portland, Oregon
Walton Laboratories, Inc.
Irvington, New Jersey
Winthrop Laboratories, Inc.
New York, New York

HOTEL RESERVATION FORM

22nd ANNUAL MEETING
AMERICAN COLLEGE OF CHEST PHYSICIANS
Hotel Sherman, Chicago, Illinois, June 7-10, 1956

The 105th Annual Meeting of the American Medical Association will immediately follow the College meeting in Chicago, June 11 through 15, 1956.

Please send this form to the Hotel Sherman at once—requests for reservations will be accepted in the order received.

Reservation Form
AMERICAN COLLEGE OF CHEST PHYSICIANS

Hotel Sherman Reservation Office
Randolph and Clark Streets, Chicago 1, Illinois

Name.....

Address.....

City..... State.....

Arrival Date..... Departure Date.....

Single Rooms		Twin Bedrooms		Suites	
$6.95	$10.95	$12.95	$15.95	$22.95	$34.95
7.45	11.95	13.45	16.95	28.95	36.95
8.95	12.95	14.95	17.95		
9.95					

Please circle approximate rate desired

Comments.....

.....

TEAR ALONG EDGE

ADVANCE REGISTRATION FORM

Urgent Notice

By completing this form and returning it at once to the Executive Offices of the College in Chicago, you will avoid having to stand in line at the Registration Desk of the annual meeting in Chicago. Your badge and program, as well as luncheon, banquet and seminar tickets, will be prepared in advance and will be waiting your arrival at the Hotel Sherman. Please complete both sides of this Advance Registration Form and mail promptly. Thank you.

Please Print

Name .....

Address .....

City and State .....

Accompanied by .....

Hotel .....

Arrival date .....

Departure date .....

I am enclosing my check in the amount of $.....for reservations as indicated on the reverse side of this form.

Remarks .....

.....

.....

Return this form to:

Executive Offices
American College of Chest Physicians
112 East Chestnut Street
Chicago 11, Illinois

Complete the coupon on reverse side

RESERVATION FORM

Seminars, Wednesday, June 6 **($7.50 each)**

MORNING SESSIONS 9 a.m. - 12 noon	AFTERNOON SESSIONS 2:00 - 5:00 p.m.
First choice A.M.....	First choice P.M.....
Second choice A.M.....	Second choice P.M.....

Please indicate choice by number as listed in program.

Round Table Luncheons **($3.50 each)**

	Friday, June 8	Saturday, June 9	Sunday, June 10
First choice	A-.....	B-.....	C-.....
Second choice	A-.....	B-.....	C-.....
Third choice	A-.....	B-.....	C-.....

Please indicate choice by number as listed in program.

Luncheon, 12th Annual College Conference **($3.50 each)**

Thursday, June 7

I wish to reserve.....tickets for the Annual College Conference, Thursday noon, June 7.

Presidents' Banquet, Saturday, June 9 **($6.50 each)**

I wish to reserve.....tickets for the Presidents' Banquet, Saturday, June 9. (price includes cocktails, dinner and dancing.)

Complete the coupon on reverse side

NOTE: Please make checks payable to *American College of Chest Physicians.* Checks must accompany all requests for reservations and will be accepted in the order in which they are received. All tickets will be held for pick-up at the College Registration Desk, Mezzanine Floor, Hotel Sherman.

TEAR ALONG EDGE

College Chapter News

ARKANSAS CHAPTER

The Arkansas Chapter will hold its annual meeting at the Marion Hotel, Little Rock, April 22. Following a social hour and dinner commencing at 6:00 p.m., Dr. David M. Gould, Little Rock, will speak on "Roentgen Findings in Lupus Erythematosus."

FLORIDA CHAPTER

The annual meeting of the Florida Chapter will take place at the Fontainebleau Hotel, Miami Beach, May 13. Dr. Hawley H. Seiler, Tampa, Chapter President, will preside at a business meeting to be held at 9:00 a.m. Dr. C. M. Sharp, Jacksonville, has arranged the following scientific program:

9:45 a.m. Morning Session—Hawley H. Seiler, presiding

Panel Discussion—"What is the Present Day Management of Pulmonary Tuberculosis?"

Moderator: Jack Reiss, Coral Gables

Sanatorium Director: B. L. Brock, Orlando

Thoracic Surgeon: L. H. Kingsbury, Orlando

Private Physician: P. W. Horn, Jacksonville

Public Health Physician: C. L. Brumback, West Palm Beach

"Evaluation of Pulmonary Function"

Philip Samet, Miami Beach; Discussion leader: George Baum, Coral Gables

"The Technique and Value of Bronchography in the Diagnosis of Pulmonary Diseases"

Robert T. Rengarts, Fort Lauderdale; Discussion leader: Ivan C. Schmidt, West Palm Beach

12:00 noon Luncheon

2:00 p.m. Afternoon Session—Jack Reiss, Vice-President, presiding

"Detection of Congenital Heart Disease by X-ray Surveys"

S. D. Doff, Jacksonville; Discussion leader: F. A. Hernandez, Miami

"The Practice of Cardiovascular Surgery in the Average Community"

Edward R. Munell, Oteen, North Carolina

"Indications for Surgery in Coronary Heart Disease"

Sidney Smith, Bradenton; Discussion leader: Franz H. Stewart, Miami

X-ray Seminar

M. Jay Flipse, Miami, Moderator (Those in attendance are requested to bring x-rays for discussion after presenting a brief and pertinent clinical history)

ILLINOIS CHAPTER

The annual meeting of the Illinois Chapter will be held at the Hotel Sherman, Chicago, May 17. The following program will be presented, commencing at 10:00 a.m. and will be concluded with a luncheon and business meeting at 12:00 noon:

Panel Discussion—"The Problem of the Patient with Irremovable Pulmonary Carcinoma"

Moderator: William M. Lees, Chicago

Panel: Harold C. Voris, Lewis Haas, Marc H. Hollender, Chicago, and William Walsh, Hines

GEORGIA CHAPTER

The Georgia Chapter will meet at the Biltmore Hotel, Atlanta, May 13-14, in conjunction with the Georgia Trudeau Society, during the meeting of the Medical Association of Georgia. Following is the chapter program:

Sunday—May 13

2:15 p.m. Thomas Findley, Augusta, presiding
"Aspects of Chest Pathology Affecting Anesthesia"
C. Ron Stephen, Durham, North Carolina
"Angiocardiography in the Diagnosis of Pulmonary Stenosis"
Wendell Scott, St. Louis, Missouri
"Indications for Cardiac Surgery"
John Kirklin, Rochester, Minnesota
"Use of Antibiotics in Chest Diseases"
John H. McClement, New York City
Panel discussion—"The Management of Thoracic Diseases During the Surgical Period"
Moderator: Thomas Findley
Participants: C. Ron Stephen, Wendell Scott, John Kirklin, John H. McClement

Monday—May 14

Luncheon, Biltmore Hotel
Speaker: John H. McClement

KANSAS CHAPTER

The annual meeting of the Kansas Chapter will be held in Topeka on May 3, in conjunction with the state medical association meeting. Dr. William Nice, Topeka, has arranged the following program:

10:00 a.m. In Sung Kwak, Topeka, presiding
"Indications for Pulmonary Resection"
John Shellito, Wichita
"Hemodynamics of Pulmonary Circulation"
James Dowell, Kansas City
"The Problem of the Treatment of the Tuberculin Converter"
Joseph B. Stocklen, Cleveland, Ohio
"Generalized Tuberculosis and Histoplasmosis"
George Post, Wadsworth

12:00 noon Luncheon

2:00 p.m. William Nice, presiding
"Practical Pulmonary Physiology"
Roy Lawson, Kansas City, Missouri
"Tuberculosis Survey in Kansas: A Preliminary Report"
Joseph B. Stocklen
"Pulmonary Tuberculosis and Malignancy"
Albert Jackson, Wadsworth
"Serum Transaminase"
Sam Zelman, Topeka
Panel Discussion—"The Treatment of Traumatic Injuries of the Chest"
Moderator: Robert Brooker, Topeka
Participants: A. L. Ashmore, Wichita; Ben H. Buck, Jr., Wichita

6:00 p.m. Social Hour

7:00 p.m. Dinner and election of officers
Guest speaker: George R. Meneely, Nashville, Tennessee

MINNESOTA CHAPTER

The Minnesota Chapter will have a luncheon meeting on May 21, Rochester, at which time the business meeting will be held.

JAPANESE CHAPTER

The annual mid-winter meeting of the Japanese Chapter was held at the Kitazato Memorial Hall of Keio University School of Medicine, Tokyo, in February. Three hundred physicians attended the scientific session at which the following program was presented:

"Clinical Observations on INH Resistant Bacilli"
Kikujo Shimamura, Tokyo

"The Combined Use of Antibiotics and Hormones for Pulmonary Tuberculosis"
Naoyoshi Hayashi, Tokyo

"Pulmonary Circulation"
Miyoshi Urabi, Kanazawa

A business meeting was held and the following officers elected:

President:	Yoneji Miyagawa, Tokyo
Vice-President:	Naoyoshi Hayashi, Tokyo
Secretary-Treasurer:	Ichiro Akakura, Tokyo

CALIFORNIA CHAPTER

The California Chapter will hold its annual meeting at the Ambassador Hotel, Los Angeles, April 28, preceding the opening day of the state medical association meeting. Dr. Samuel J. Sills, Los Angeles, has arranged the following program:

9:00 a.m. Registration

9:30 a.m. Morning Session—Walter B. Brown, Livermore, Presiding

"'Pembine' Type Conference"
Moderator: David Salkin, San Fernando (Presentation of an unselected group of cases from the last 50 discharges immediately preceding February 1, 1954 at the Veterans Administration Hospital, San Fernando)

"Interesting Cases I have Seen—What Would be Your Modus Operandi?"
Moderator: Elmer Rigby, Los Angeles
Participants: Marvin S. Harris, Los Angeles; William G. Winter, Fresno; Harold G. Trimble, Oakland; Stephen R. Elek, Los Angeles; Thomas B. Wiper, San Francisco

12:00 noon Luncheon—Coconut Grove
Business meeting and presentation of chapter's annual award by Alfred Goldman, Beverly Hills

2:00 p.m. "Disturbances of the Vascular Pattern of the Lung"
Leo G. Rigler, Duarte

"Collateral Coronary Circulation—The Effect of Systemic Blood Pressure on Coronary Circulation"
Lauro B. de Vera, Herbert Gold, and Eliot Corday, Los Angeles

"Surgery of Thoracic Aortic Aneurysms"
Sanford Leeds, San Francisco

"Little-Known Problems of Angina Pectoris"
David Scherf, New York City

"Respiratory Acidosis"
James Kieran, Oakland

"Diagnostic Procedures—New and Review"

1. Agammaglobulinemia
   Thomas Brem, Los Angeles
2. Transanimase in Heart Disease
   Clarence Agress, Los Angeles
3. Bone Marrow Studies in Pulmonary Disease
   Irwin Weinstein, Los Angeles
4. Liver Biopsy in Chest Diseases
   William Molle, Los Angeles and Melvin Brody, Sawtelle
5. All Acid-Fast Are not Tubercle Bacilli
   Lawrence G. Wayne, Ph.D., Milton Ruppert, Ph.D., and William J. Jaurez, M.T., San Fernando

5.30 p.m. Social Hour

MICHIGAN CHAPTER

The Michigan Chapter held its annual meeting on February 15, Detroit. Dr. W. L. Howard, Northville, presented an illustrated survey of the readmitted cases at the Maybury Sanatorium during 1955, showing that 45 per cent of all adult admissions had been treated previously, that 64 per cent of re-treatment cases had absconded from previous treatment, and that they were mainly unmarried men, unskilled workers and alcoholics. Following the scientific session, a business meeting was held at which the following officers were elected:

President:	Kenneth A. Wood, Detroit
Vice-President:	W. L. Howard, Northville
Secretary-Treasurer:	Stephen M. Gelenger, Flint
Program Committee:	James T. Cheng, Pontiac
	Nathan Levitt, Detroit

NEW ENGLAND STATES CHAPTER

At the regular monthly meeting of the New England States Chapter, held on February 15, Boston, Dr. Walter T. Goodale, Boston, spoke on "The Role of Pulmonary Vascular Disease in Atrial Septal Defects and Patent Ductus Arteriosus." Dr. Emil Rothstein, Brockton, Massachusetts, reported on "The Fifteenth Conference of the Chemotherapy of Tuberculosis" (Veterans Administration, Army, and Navy) at the March 21 meeting of the Chapter.

NEW JERSEY CHAPTER

The New Jersey Chapter will present the program for the Chest Section of the state medical society on May 16, Atlantic City. Dr. Emanuel Klosk, Newark, has prepared the following program:

"Cytological Patterns in Bronchopulmonary Disease"
A. A. Carabelli, Trenton

"A Survey of 900 Consecutive Cases of Myocardial Infarction"
I. L. Applebaum, Newark

"An Analysis of 100 Cases of Tuberculosis Treated at Home"
Benjamin P. Potter, Jersey City

"Trauma to the Chest"
Ross J. Simpson, Bayonne

"Serial Tomography in the Chemotherapeutic Management of Pulmonary Tuberculosis"
Irving J. Selikoff, David Roth, and Robert Joelson, Paterson

NEW YORK CHAPTER

The Sixteenth Annual Dinner Meeting of the New York State Chapter will be held at the Hotel Statler, New York City, May 10, at which Dr. Ethan Flagg Butler, Elmira, will present the Sixth Annual Howard Lilienthal Lecture entitled "Howard Lilienthal—Father of Lobectomy."

PENNSYLVANIA CHAPTER

The annual meeting of the Pennsylvania Chapter will be held at Mont Alto Sanatorium, South Mountain, May 4. The Program Chairman, Dr. M. C. Stayer, Harrisburg, has arranged the following program:

11:00 a.m. Moderator: M. C. Stayer

"Pneumoconioses"
Eugene Pendergrass, Philadelphia; Discussion leader: John S. Packard, Allenwood

"Silicosis"
Ross K. Childerhose, Harrisburg; Discussion leader: R. H. McCutcheon, Hamburg

12:30 p.m. Luncheon

1:30 p.m. "Present Day Management of Coin Lesions"
Robert L. Mayock, Philadelphia; Discussion leader: Robert P. Glover, Philadelphia

"Present Status of Chemotherapy in Tuberculosis"
Martin J. Sokoloff, Philadelphia; Discussion leader: R. S. Anderson, Erie

3:00 p.m. Business meeting and election of officers

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Gerald L. Crenshaw, M.D., Oakland
Glenroy N. Pierce, M.D., San Francisco
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Robert Stone, M.D., Oakland
William B. Leftwich, M.D., Oakland

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CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

22nd Annual Meeting, American College of Chest Physicians
Hotel Sherman, Chicago, Illinois, June 7-10, 1956

Fourth International Congress on Diseases of the Chest
Council on International Affairs, American College of Chest Physicians
Cologne, Germany, August 19-23, 1956

CHAPTER MEETINGS

Arkansas Chapter, Little Rock, April 22, 1956
California Chapter, Los Angeles, April 28, 1956
Kansas Chapter, Topeka, May 3, 1956
Pennsylvania Chapter, South Mountain, May 4, 1956
Mississippi Chapter, Jackson, May 7, 1956
New York Chapter, New York City, May 10, 1956
Florida Chapter, Miami Beach, May 13, 1956
Georgia Chapter, Atlanta, May 13-14, 1956
New Jersey Chapter, Atlantic City, May 16, 1956
Illinois Chapter, Chicago, May 17, 1956
Minnesota Chapter, Rochester, May 21, 1956

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1. Burrascano, J. J.: Sea View Hosp. Bull. *15*:149 (July) 1955.

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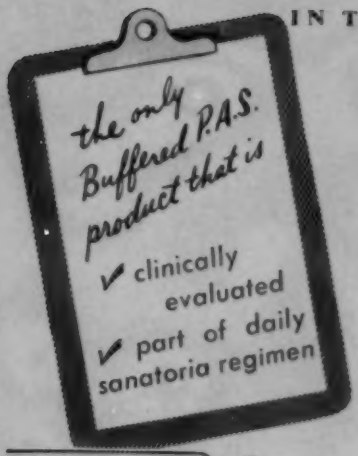

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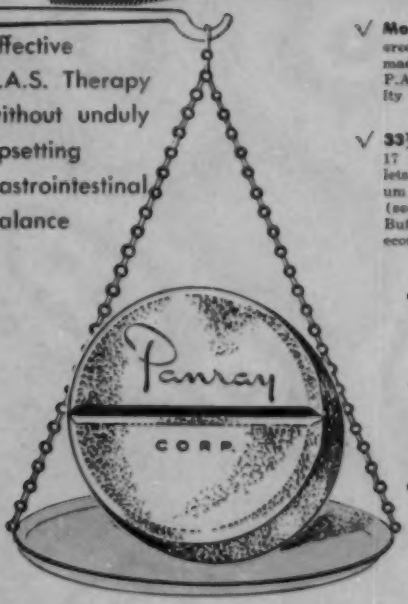

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